



Gaps - 0 Conservative Substitutions - 0

X X  
PGPIH  
|||||  
PGPIH  
X X

2. US-09-095-639A-1 (1-5)  
aaw31287 Bovine beta casein variant A1 immunogenic peptide

TOIG of: aaw31287 check: 1114 from: 1 to: 5

ID AAW31287 standard; peptide; 5 AA.

XX AAW31287;

AC AAW31287;

DT 05-MAR-1998 (first entry)

XX Bovine beta casein variant A1 immunogenic peptide motif.

KW A1 variant beta casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.

XX Bos taurus.

XX WO9724371-A1.

XX 10-JUL-1997.

XX 27-DEC-1996; 96WO-EP05846.

XX 27-DEC-1995; 95IT-ORW0850.

XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
XX (MIDI-) MIDIA LTD.

XX Pozzilli P;

XX WPI; 1997-363622/33.

XX Beta-casein or fragments not showing mimicry with GLUT2 - used in  
XX food or pharmaceutical products for prevention of insulin dependent  
XX diabetes, particularly in early infancy

XX Claim 5; Page 3; 34pp; English.

XX This sequence represents an immunogenic peptide motif from the A1  
XX variant of beta-casein which is capable of mimicking a fragment of the  
XX GLUT2 protein found in insulin producing cells of the pancreas. There is  
XX a known correlation between exposure to cow's milk and the development of  
XX insulin-dependent diabetes which could possibly be linked to this  
XX molecular mimicry. Dietary or pharmaceutical products derived from milk  
XX substantially free of non-human beta casein or containing modified  
XX beta-casein without this motif could be used in diets for the prevention  
XX of insulin dependent diabetes particularly during early infancy.

XX Sequence 5 AA;

AAW31287 Length: 5 March 3, 2003 11:29 Type: P Check: 1114

Initial Score = 5 Optimized Score = 5 Significance = 1.11  
Residue Identity = 100% Matches = 5 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIH  
|||||  
PGPIH  
X X

3. US-09-095-639A-1 (1-5)  
R95609 Bovine beta casein A1 variant.

ID R95609 standard; protein; 209 AA.

AC R95609;

DT 26-NOV-1996 (first entry)

DE Bovine beta casein A1 variant.

KW Milk; beta casein; diabetogenic; diabetes; cow; milk products;

KW butter; cheese; cream.

OS Bos taurus.

FH Key Location/Qualifiers

FT region 63..68

FT /label= Diabetogenic hexapeptide.

PN WO9614577-A1.

PD 17-MAY-1996.

PF 03-NOV-1995; NZ0114.

PR 04-NOV-1994; NZ-264862.

PA (NACH-) NAT CHILD HEALTH RES FOUND.

PA (NZDA-) NEW ZEALAND DAIRY BOARD.

PI Elliott RB, Hill JP;

DR WPI; 96-251885/25.

PT Selecting non-diabetogenic milk and milk prods. - by testing milk or  
PT cows for the presence of non-diabetogenic variants of beta-casein  
PS Disclosure; Figure 2; 28pp; English.  
CC A method for selecting milk for feeding to diabetes susceptible  
CC individuals comprises testing milk from identified cows for the  
CC presence of variants of beta casein and selecting those cows whose  
CC milk contains non-diabetogenic variants and milking these cows  
CC separately. The milk and milk products obtained can reduce the risk  
CC of susceptible individuals contracting type-1 diabetes.

SQ Sequence 209 AA;

SQ 5 A; 4 R; 4 N; 5 D; 0 B; 0 C; 21 Q; 18 E; 0 Z; 5 G; 6 H;

SQ 10 I; 22 L; 11 K; 6 M; 9 F; 34 P; 16 S; 9 T; 1 W; 4 Y; 19 V;

SQ retrieved by bobryen on Thu 27 Feb 103 16:22:05-PST using FindSeq

Initial Score = 5 Optimized Score = 5 Significance = 1.11  
Residue Identity = 100% Matches = 5 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIH  
|||||

AQTQSLVYPPFPPIHNSLPQNIPL

60 X X 70

4. US-09-095-639A-1 (1-5)

R80281 Methyl or ethyl esterified bovine beta-casein A1.

ID R80281 standard; protein; 209 AA.

AC R80281;

DT 14-FEB-1996 (first entry)

DE Methyl or ethyl esterified bovine beta-casein A1.

KW Bovine; beta-casein; ethyl esterification; pepsin hydrolysis;

KW proteolysis; peptide ester; food; pharmaceutical; cosmetics.

OS Bos taurus.

FH Key Location/Qualifiers

FT protein 1..209

FT /note= "55% esterified by methanol or by

FT ethanol, resulting in atypical pepsin

FT cleavage sites, in addition to the

FT naturally occurring (native) sites"

FT cleavage\_site 4..5

FT /note= "pepsin cleavage site in native protein"

FT cleavage\_site 5..6

FT /note= "pepsin cleavage site in native protein and

FT in methyl ester of beta-casein"

FT cleavage\_site 11..12

FT /note= "newly identified pepsin cleavage site in

FT methyl ester of beta-casein"

FT cleavage\_site 15..16

FT /note= "pepsin cleavage site in native protein"

FT cleavage\_site 44..45



PGPIH  
|||||  
AQTQSLVYPPFGPIHNSLPQNIPPL  
60 X X 70

5. US-09-095-639A-1 (1-5)  
aar95609 Bovine beta casein Al variant.

TOIG of: aar95609 check: 2014 from: 1 to: 209

ID AAR95609 standard; protein; 209 AA.

XX AC AAR95609;

XX DT 26-NOV-1996 (first entry)

XX DE Bovine beta casein Al variant.

XX KW Milk; beta casein; diabetogenic; diabetes; cow; milk products;  
butter; cheese; cream.

XX BO Bos taurus.

XX FH Key Location/Qualifiers  
XX FT Region 63.68  
XX FT /label= Diabetogenic hexapeptide.

XX PN WO9614577-Al.

XX PD 17-MAY-1996.

XX PF 03-NOV-1995; 95WO-NZ001114.

XX PR 04-NOV-1994; 94NZ-0264862.

XX PA (NACH-) NAT CHILD HEALTH RES FOUND.

XX PA (NZDA-) NEW ZEALAND DAIRY BOARD.

XX PI Elliott RB, Hill JP;

XX DR WPI; 1996-251885/25.

XX PT Selecting non-diabetogenic milk and milk prods. - by testing milk or  
cows for the presence of non-diabetogenic variants of beta-casein

XX PS Disclosure; Figure 2; 28pp; English.

XX CC A method for selecting milk for feeding to diabetes susceptible  
individuals comprises testing milk from identified cows for the  
presence of variants of beta casein and selecting those cows whose  
milk contains non-diabetogenic variants and milking these cows  
separately. The milk and milk products obtained can reduce the risk  
of susceptible individuals contracting Type-1 diabetes.

XX SQ Sequence 209 AA;

AAR95609 Length: 209 March 3, 2003 11:28 Type: P Check: 2014

Initial Score = 5 Optimized Score = 1.11  
Residue Identity = 100% Matches = 5 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0

XX X  
XX PGPIH  
XX |||||

AQTQSLVYPPFGPIHNSLPQNIPPL  
60 X X 70

6. US-09-095-639A-1 (1-5)  
W31289 Bovine beta casein variant Al immunogenic peptide.

ID W31289 standard; peptide; 12 AA.  
AC W31289;  
DT 05-MAR-1998 (first entry)  
DE Bovine beta casein variant Al immunogenic peptide.  
KW Al variant beta casein; immunogenic; molecular mimicry; cow;  
milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
PN WO9724371-Al.  
PD 10-JUL-1997.  
PF 27-DEC-1996; E05846.  
PR 27-DEC-1995; IT-RM0850.  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
PI Pozzilli P;  
DR WPI; 97-363622/33.  
PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
PS Claim 5; Page 3; 34pp; English.  
CC This sequence represents an immunogenic peptide from the Al variant of  
CC beta-casein which contains a motif (see W31287) capable of mimicking a  
CC fragment of the GLUT2 protein found in insulin producing cells of the  
CC pancreas. There is a known correlation between exposure to cow's milk and  
CC the development of insulin-dependent diabetes which could possibly be  
CC linked to this molecular mimicry. Dietary or pharmaceutical products  
CC derived from milk substantially free of non-human beta casein or  
CC containing modified beta-casein without this motif could be used in diets  
CC for the prevention of insulin dependent diabetes particularly during  
CC early infancy.  
SQ Sequence 12 AA;  
SQ 0 A; 0 R; 1 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 1 H;  
SQ 1 I; 1 L; 0 K; 0 M; 1 F; 3 P; 1 S; 0 T; 0 W; 1 Y; 1 V;  
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq  
Initial Score = 5 Optimized Score = 1.11  
Residue Identity = 100% Matches = 5 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0  
XX X  
XX PGPIH  
XX |||||  
XX SLVYPPFGPIHN  
XX X 10

7. US-09-095-639A-1 (1-5)  
aaw31289 Bovine beta casein variant Al immunogenic peptide.

TOIG of: aaw31289 check: 5975 from: 1 to: 12

ID AAW31289 standard; peptide; 12 AA.

XX AC AAW31289;

XX DT 05-MAR-1998 (first entry)

XX DE Bovine beta casein variant Al immunogenic peptide.

XX KW Al variant beta casein; immunogenic; molecular mimicry; cow;  
milk product; insulin-dependent diabetes; GLUT2; diet.  
XX OS Bos taurus.

XX PN WO9724371-Al.

XX PD 10-JUL-1997.

XX PF 27-DEC-1996; 96WO-EP05846.

XX PR 27-DEC-1995; 95IT-ORM0850.

XX PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.

XX Pozzilli P;  
 XX WPI; 1997-363622/33.  
 XX Beta-casein or fragments not showing mimicry with GLUT2 - used in  
 PT food or pharmaceutical products for prevention of insulin dependent  
 PT diabetes, particularly in early infancy  
 XX Claim 5; Page 3; 34pp; English.  
 XX This sequence represents an immunogenic peptide from the A1 variant of  
 CC beta-casein which contains a motif (see AAW31287) capable of mimicking a  
 CC fragment of the GLUT2 protein found in insulin producing cells of the  
 CC pancreas. There is a known correlation between exposure to cow's milk  
 CC and the development of insulin-dependent diabetes which could possibly  
 CC be linked to this molecular mimicry. Dietary or pharmaceutical products  
 CC derived from milk substantially free of non-human beta casein or  
 CC containing modified beta-casein without this motif could be used in  
 CC diets for the prevention of insulin dependent diabetes particularly  
 XX during early infancy.  
 XX SQ Sequence 12 AA;

AAW31289 Length: 12 March 3, 2003 11:28 Type: P Check: 5975  
 Initial Score = 5 Optimized Score = 1.11  
 Residue Identity = 100% Matches = 5 Mismatches = 0  
 Gaps = 0 Conservative Substitutions = 0

X X  
 PGPIH  
 ||||  
 SLVYFPFGPIH  
 X 10

8. US-09-095-639A-1 (1-5)  
 W31293 Bovine beta casein immunogenic peptide motif 1.

ID W31293 standard; peptide; 4 AA.  
 AC W31293;  
 DT 05-MAR-1998 (first entry)  
 DE Bovine beta casein immunogenic peptide motif 1.  
 KW Beta casein; immunogenic; molecular mimicry; cow;  
 OS milk product; insulin-dependent diabetes; GLUT2; diet.  
 OS Bos taurus.  
 WO9724371-A1.  
 10-JUL-1997.  
 27-DEC-1996; E05846.  
 PR 27-DEC-1995; IT-RM0850.  
 PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
 PA (MIDI-) MIDIA LTD.  
 PI Pozzilli P;  
 DR WPI; 97-363622/33.  
 PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
 PT food or pharmaceutical products for prevention of insulin dependent  
 PT diabetes, particularly in early infancy  
 PS Claim 10; Page 6; 34pp; English.  
 CC This sequence represents an immunogenic peptide motif of beta-casein  
 CC which is capable of mimicking a fragment of the GLUT2 protein found in  
 CC insulin producing cells of the pancreas. There is a known correlation  
 CC between exposure to cow's milk and the development of insulin-dependent  
 CC diabetes which could possibly be linked to this molecular mimicry.  
 CC Dietary or pharmaceutical products derived from milk substantially free  
 CC of non-human beta casein or containing modified beta-casein without this  
 CC motif could be used in diets for the prevention of insulin dependent  
 CC diabetes particularly during early infancy.  
 XX Sequence 4 AA;

SQ 0 A; 0 R; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 1 H;  
 SQ 1 I; 0 L; 0 K; 0 M; 0 F; 1 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
 CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 4 Optimized Score = 4 Significance = 0.00  
 Residue Identity = 100% Matches = 4 Mismatches = 0  
 Gaps = 0 Conservative Substitutions = 0

X X  
 PGPIH  
 ||||  
 GPIH  
 X X

9. US-09-095-639A-1 (1-5)  
 aaw31293 Bovine beta casein immunogenic peptide motif 1.

TOIG of: aaw31293 check: 738 from: 1 to: 4

ID AAW31293 standard; peptide; 4 AA.

XX AAW31293;

XX 05-MAR-1998 (first entry)

XX Bovine beta casein immunogenic peptide motif 1.

XX Beta casein; immunogenic; molecular mimicry; cow;  
 KW milk product; insulin-dependent diabetes; GLUT2; diet.

OS Bos taurus.

XX WO9724371-A1.

XX 10-JUL-1997.

XX 27-DEC-1996; 96WO-EF05846.

XX 27-DEC-1995; 95IT-ORM0850.

XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
 PA (MIDI-) MIDIA LTD.

XX Pozzilli P;

XX WPI; 1997-363622/33.

XX Beta-casein or fragments not showing mimicry with GLUT2 - used in  
 PT food or pharmaceutical products for prevention of insulin dependent  
 PT diabetes, particularly in early infancy

XX Claim 10; Page 6; 34pp; English.

XX This sequence represents an immunogenic peptide motif of beta-casein  
 CC which is capable of mimicking a fragment of the GLUT2 protein found in  
 CC insulin producing cells of the pancreas. There is a known correlation  
 CC between exposure to cow's milk and the development of insulin-dependent  
 CC diabetes which could possibly be linked to this molecular mimicry.  
 CC Dietary or pharmaceutical products derived from milk substantially free  
 CC of non-human beta casein or containing modified beta-casein without this  
 CC motif could be used in diets for the prevention of insulin dependent  
 CC diabetes particularly during early infancy.

XX Sequence 4 AA;

AAW31293 Length: 4 March 3, 2003 11:29 Type: P Check: 738

Initial Score = 4 Optimized Score = 4 Significance = 0.00  
 Residue Identity = 100% Matches = 4 Mismatches = 0  
 Gaps = 0 Conservative Substitutions = 0

X X  
 PGPIH  
 ||||  
 GPIH  
 X X

10. US-09-095-639A-1 (1-5)  
W31288 Bovine beta casein variant A2 immunogenic peptide

ID W31288 standard; peptide; 5 AA.  
AC W31288; 1998 (first entry)  
DE Bovine beta casein variant A2 immunogenic peptide motif.  
KW A2 variant beta-casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
OS Bos indicus.  
PN WO9724371-AL.  
PD 10-JUL-1997.  
PF 27-DEC-1996; E05846.  
PR 27-DEC-1995; IT-RM0850.  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
PI Pozzilli P;  
DR WPI; 97-363622/33.  
CC Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy  
PS Claim 5; Page 4; 34pp; English.  
CC This sequence represents an immunogenic peptide motif from the A2 variant beta-casein found in both Bos taurus and Bos indicus (amino acid position 63-68). This motif is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.  
SQ Sequence 5 AA;  
SQ 1 I; 0 L; 0 K; 0 M; 0 P; 3 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07 PST using FindSeq

Initial Score = 4 Optimized Score = 4 Significance = 0.00  
Residue Identity = 80% Matches = 4 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIH  
||||  
PGPIP  
X X

11. US-09-095-639A-1 (1-5)  
aaw31288 Bovine beta casein variant A2 immunogenic peptide

TOIG of: aaw31288 check: 1154 from: 1 to: 5

ID AAW31288 standard; peptide; 5 AA.

AC AAW31288;

DE 05-MAR-1998 (first entry)

DR Bovine beta casein variant A2 immunogenic peptide motif.

PT A2 variant beta-casein; immunogenic; molecular mimicry; cow;  
PT milk product; insulin-dependent diabetes; GLUT2; diet.  
PS Bos taurus.  
CC Bos indicus  
CC WO9724371-AL.  
CC 10-JUL-1997.

XX  
PF  
XX  
PR  
XX  
PA  
PA  
XX  
PI  
XX  
DR  
XX  
PT  
PT  
XX  
PS  
XX  
CC  
CC  
CC  
CC  
CC  
CC  
CC  
XX  
SQ

27-DEC-1996; 96WO-EP05846.  
27-DEC-1995; 95IT-ORM0850.  
(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
(MIDI-) MIDIA LTD.  
Pozzilli P;  
WPI; 1997-363622/33.

Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

Claim 5; Page 4; 34pp; English.

This sequence represents an immunogenic peptide motif from the A2 variant beta-casein found in both Bos taurus and Bos indicus (amino acid position 63-68). This motif is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

Sequence 5 AA;

AAW31288 Length: 5 March 3, 2003 11:28 Type: P Check: 1154

Initial Score = 4 Optimized Score = 4 Significance = 0.00  
Residue Identity = 80% Matches = 4 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIH  
||||  
PGPIP  
X X

12. US-09-095-639A-1 (1-5)  
W31290 Bovine beta casein variant A2 immunogenic peptide.

ID W31290 standard; peptide; 12 AA.

AC W31290;

DE 05-MAR-1998 (first entry)

DE Bovine beta casein variant A2 immunogenic peptide.

KW A2 variant beta-casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.

OS Bos taurus.  
OS Bos indicus.  
PN WO9724371-AL.  
PD 10-JUL-1997.  
PF 27-DEC-1996; E05846.  
PR 27-DEC-1995; IT-RM0850.  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
PI Pozzilli P;  
DR WPI; 97-363622/33.

Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy  
Claim 5; Page 4; 34pp; English.  
This sequence represents an immunogenic peptide from the A2 variant of beta-casein found in both Bos taurus and Bos indicus. The peptide contains a motif (see W31288) corresponding to amino acids 63-68 of the A2 beta casein protein and is found to be capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the

development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

Sequence 12 AA;  
SQ 0 A; 0 R; 1 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 0 H;  
SQ 1 A; 1 L; 0 K; 0 M; 1 F; 4 P; 1 S; 0 T; 0 W; 1 Y; 1 V;  
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 4 Optimized Score = 0.00  
Residue Identity = 80% Matches = 4 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIH  
||||  
SLVYPPFGPIPN  
X 10

13. US-09-095-639A-1 (1-5)  
aaw31290 Bovine beta casein variant A2 immunogenic peptide.

TOIG of: aaw31290 check: 6063 from: 1 to: 12

ID AAW31290 standard; peptide; 12 AA.

XX AAW31290;  
AC AAW31290;  
DT 21-JUL-1986 (Rel. 01, Created)  
DT 01-MAR-1989 (Rel. 10, Last sequence update)  
DT 01-MAR-2002 (Rel. 41, Last annotation update)  
DE Beta casein precursor.  
DE CSN2.  
DE Bos taurus (Bovine).  
DE Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;  
DE Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;  
DE Bovidae; Bovinae; Bos.  
DE NCBI\_TaxID=9913;  
DE [1]  
DE SEQUENCE FROM N.A.  
DE Baev A.A., Smirnov I.K., Gorodetsky S.I.;  
DE "Primary structure of bovine beta-casein CDNA."  
DE Mol. Biol. (Mosk) 21:214-222(1987).  
DE [2]  
DE SEQUENCE FROM N.A.  
DE MEDLINE=88188989; PubMed=2833669;  
DE Stewart A.F., Bonsing J., Beattie C.W., Shah F., Willis I.M.,  
DE Mackinlay A.G.;  
DE "Complete nucleotide sequences of bovine alpha S2- and beta-casein  
DE cDNAs: comparisons with related sequences in other species."  
DE Mol. Biol. Evol. 4:231-241(1987).  
DE [3]  
DE SEQUENCE FROM N.A.  
DE MEDLINE=90147279; PubMed=3271384;  
DE Bonsing J., Ring J.M., Stewart A.F., Mackinlay A.G.;  
DE "Complete nucleotide sequence of the bovine beta-casein gene."  
DE Aust. J. Biol. Sci. 41:527-537(1988).  
DE [4]  
DE SEQUENCE FROM N.A.  
DE MEDLINE=87128158; PubMed=3814153;  
DE Jimenez-Flores R., Kang Y.C., Richardson T.;  
DE "Cloning and sequence analysis of bovine beta-casein CDNA."  
DE Biochem. Biophys. Res. Commun. 142:617-621(1987).  
DE [5]  
DE SEQUENCE FROM N.A. (VARIANT A3).  
DE TISSUE=Mammary gland;  
DE MEDLINE=94068382; PubMed=8248100;  
DE Simons G., van den Heuvel W., Reynen T., Frijters A., Rutten G.,  
DE Slangen C.J., Groenen M., de Vos W.M., Siezen R.J.;  
DE "Overproduction of bovine beta-casein in Escherichia coli and  
DE engineering of its main chymosin cleavage site."  
DE protein Eng. 6:763-770(1993).  
DE [6]  
DE SEQUENCE OF 16-224 (VARIANT A2).  
DE MEDLINE=88152252; PubMed=3278933;  
DE Carles C., Huet J.-C., Ribadeau-Dumas B.;  
DE "A new strategy for primary structure determination of proteins:  
DE for the prevention of insulin dependent diabetes particularly during

CC early infancy.  
XX  
SQ Sequence 12 AA;

AAW31290 Length: 12 March 3, 2003 11:29 Type: P Check: 6063

Initial Score = 4 Optimized Score = 0.00  
Residue Identity = 80% Matches = 4 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIH  
||||  
SLVYPPFGPIPN  
X 10

14. US-09-095-639A-1 (1-5)  
p02666 Beta casein precursor.

TOIG of: p02666 check: 8112 from: 1 to: 224

ID CASB\_BOVIN STANDARD; PRT; 224 AA.  
AC P02666;  
DT 21-JUL-1986 (Rel. 01, Created)  
DT 01-MAR-1989 (Rel. 10, Last sequence update)  
DT 01-MAR-2002 (Rel. 41, Last annotation update)  
DE Beta casein precursor.  
DE CSN2.  
DE Bos taurus (Bovine).  
DE Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;  
DE Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;  
DE Bovidae; Bovinae; Bos.  
DE NCBI\_TaxID=9913;  
DE [1]  
DE SEQUENCE FROM N.A.  
DE Baev A.A., Smirnov I.K., Gorodetsky S.I.;  
DE "Primary structure of bovine beta-casein CDNA."  
DE Mol. Biol. (Mosk) 21:214-222(1987).  
DE [2]  
DE SEQUENCE FROM N.A.  
DE MEDLINE=88188989; PubMed=2833669;  
DE Stewart A.F., Bonsing J., Beattie C.W., Shah F., Willis I.M.,  
DE Mackinlay A.G.;  
DE "Complete nucleotide sequences of bovine alpha S2- and beta-casein  
DE cDNAs: comparisons with related sequences in other species."  
DE Mol. Biol. Evol. 4:231-241(1987).  
DE [3]  
DE SEQUENCE FROM N.A.  
DE MEDLINE=90147279; PubMed=3271384;  
DE Bonsing J., Ring J.M., Stewart A.F., Mackinlay A.G.;  
DE "Complete nucleotide sequence of the bovine beta-casein gene."  
DE Aust. J. Biol. Sci. 41:527-537(1988).  
DE [4]  
DE SEQUENCE FROM N.A.  
DE MEDLINE=87128158; PubMed=3814153;  
DE Jimenez-Flores R., Kang Y.C., Richardson T.;  
DE "Cloning and sequence analysis of bovine beta-casein CDNA."  
DE Biochem. Biophys. Res. Commun. 142:617-621(1987).  
DE [5]  
DE SEQUENCE FROM N.A. (VARIANT A3).  
DE TISSUE=Mammary gland;  
DE MEDLINE=94068382; PubMed=8248100;  
DE Simons G., van den Heuvel W., Reynen T., Frijters A., Rutten G.,  
DE Slangen C.J., Groenen M., de Vos W.M., Siezen R.J.;  
DE "Overproduction of bovine beta-casein in Escherichia coli and  
DE engineering of its main chymosin cleavage site."  
DE protein Eng. 6:763-770(1993).  
DE [6]  
DE SEQUENCE OF 16-224 (VARIANT A2).  
DE MEDLINE=88152252; PubMed=3278933;  
DE Carles C., Huet J.-C., Ribadeau-Dumas B.;  
DE "A new strategy for primary structure determination of proteins:  
DE for the prevention of insulin dependent diabetes particularly during

RT application to bovine beta-casein.";  
RL FEBS Lett. 229:265-272(1988).  
RN [7]  
RP SEQUENCE OF 16-224 (VARIANT A2).  
RX MEDLINE=7233212; PubMed=4557764;  
RA Ribadeau-Dumas B., Brignon G., Grosclaude F., Mercier J.-C.;  
RT "Primary structure of bovine beta casein. Complete sequence.";  
RL Eur. J. Biochem. 25:505-514(1972).  
RN [8]  
RP VARIANTS A1; B AND C.  
RX MEDLINE=72214259; PubMed=5064450;  
RA Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;  
RT "Characterization of genetic variants of alpha-S1 and beta bovine  
RT caseins.";  
RL Eur. J. Biochem. 26:328-337(1972).  
RN [9]  
RP SEQUENCE OF 118-124 (VARIANT A3).  
RX MEDLINE=71252171; PubMed=4997616;  
RA Ribadeau-Dumas B., Grosclaude F., Mercier J.-C.;  
RT "Localization in the peptide chain of bovine beta casein of the  
RT His-Gln substitution differentiating the A2 and A3 genetic  
RT variants.";  
RL C. R. Acad. Sci., D, Sci. Nat. 270:2369-2372(1970).  
RN [10]  
RP SEQUENCE OF 48-63 (VARIANT E).  
RX MEDLINE=75005247; PubMed=4411121;  
RA Grosclaude F., Mahe M.-F., Voglino G.-F.;  
RT "The beta E variant and the phosphorylation code of bovine caseins.";  
RL FEBS Lett. 45:3-5(1974).  
RN [11]  
RP SEQUENCE OF 68-105 FROM N.A.  
RX MEDLINE=85155504; PubMed=6397405;  
RA Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,  
RA Silimova G.E., Judinkova E.S., Gorodetsky S.I.;  
RT "Identification of bacterial clones encoding bovine caseins by direct  
RT immunological screening of the cDNA library.";  
RL Gene 32:381-388(1984).  
RN [12]  
RP SEQUENCE OF 68-95 FROM N.A.  
RX MEDLINE=86014005; PubMed=3900695;  
RA Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,  
RA Silimova G.E.;  
RT "Identification of bacterial clones coding for bovine caseins by  
RT direct immunologic screening of the cDNA library.";  
RL Mol. Biol. (Mosk) 19:955-963(1985).  
RN [13]  
RP SEQUENCE OF 18-57 FROM N.A., AND SEQUENCE OF 16-224 (VARIANT H).  
RX MEDLINE=20154951; PubMed=10690361;  
RA Han S.K., Shin Y.C., Byun H.D.;  
RT "Biochemical, molecular and physiological characterization of a new  
RT beta-casein variant detected in Korean cattle.";  
RL Anim. Genet. 31:49-51(2000).  
RN [14]  
RP SEQUENCE OF 125-195 (VARIANTS A1 AND G).  
RX Dong C., Ng-Kwai-Hang K.F.;  
RT "Characterization of a non-electrophoretic genetic variant of beta-  
RT casein by peptide mapping and mass spectrometric analysis.";  
RL Int. Dairy J. 8:967-972(1998).  
RN [15]  
RP SEQUENCE OF 160-171 (VARIANT F).  
RX MEDLINE=96118672; PubMed=7496485;  
RA Visser S., Slangen C.J., Lagerwerf F.M., Van Dongen W.D.,  
RA Haverkamp J.;  
RT "Identification of a new genetic variant of bovine beta-casein using  
RT reversed-phase high-performance liquid chromatography and mass  
RT spectrometric analysis.";  
RL J. Chromatogr. A 711:141-150(1995).  
RN [16]  
RP SEQUENCE OF 170-184 FROM N.A.  
RX MEDLINE=83182023; PubMed=6897774;  
RA Willis I.M., Stewart A.F., Caputo A., Thompson A.R., McKinlay A.G.;  
RT "Construction and identification by partial nucleotide sequence  
RT analysis of bovine casein and beta-lactoglobulin cDNA clones.";  
RN [17]  
DNA 1:375-386(1982).  
RL [17]  
RP CARBOHYDRATE-LINKAGE SITES.  
RX MEDLINE=85000478; PubMed=6148101;  
RA Yan S.B., Wold F.;  
RT "Neoglycoproteins: in vitro introduction of glycosyl units at  
RT glutamines in beta-casein using transglutaminase.";  
RL Biochemistry 23:3759-3765(1984).  
CC -1- FUNCTION: IMPORTANT ROLE IN DETERMINATION OF THE SURFACE  
CC PROPERTIES OF THE CASEIN MICELLES.  
CC -1- SUBCELLULAR LOCATION: Extracellular.  
CC -1- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.  
CC -1- POLYMORPHISM: LEU-152 IS PRESENT IN THE VARIANTS F AND G; GLN-190  
CC AND GLU-210 ARE PRESENT IN THE VARIANT H. THE SEQUENCE SHOWN IS  
CC THE A2 VARIANT.  
CC -1- SIMILARITY: BELONGS TO THE BETA-CASEIN FAMILY.  
CC -1- DATABASE: NAME-Protein Spotlight;  
CC NOTE=Issue 16 of November 2001;  
CC WWW="http://www.expasy.org/spotlight/articles/sptl016.html".  
CC -----  
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CC or send an email to license@isb-sib.ch).  
CC -----  
DR EMBL; M16645; AAA30480.1; -  
DR EMBL; M15132; AAA30430.1; -  
DR EMBL; K01087; AAA30481.1; -  
DR EMBL; X06359; AAA29658.1; -  
DR EMBL; M5158; AAA30431.1; -  
DR EMBL; S67277; AAB29137.1; -  
DR EMBL; AF104929; AAD09813.1; -  
DR EMBL; AF104928; AAD09813.1; JOINED.  
DR EMBL; M64756; AAB59254.1; -  
DR PIR; A03110; KB0A2.  
DR PIR; A25846; A25846.  
DR PIR; B29087; B29087.  
DR PIR; S01860; S01860.  
DR PIR; S02429; S02429.  
DR Carlsberg; CCSD:9067; -  
DR InterPro; IPR001588; Casein.  
DR Pfam; PF00363; caseins; 1.  
DR PROSITE; PS00306; CASEIN ALPHA\_BETA; 1.  
KW Milk; Phosphorylation; Glycoprotein; Signal; Polymorphism.  
FT SIGNAL 1 15  
FT CHAIN 16 224  
FT MOD\_RES 30 30 BETA CASEIN.  
FT MOD\_RES 32 32 PHOSPHORYLATION.  
FT MOD\_RES 33 33 PHOSPHORYLATION.  
FT MOD\_RES 34 34 PHOSPHORYLATION.  
FT MOD\_RES 50 50 PHOSPHORYLATION (EXCEPT IN VARIANT C).  
FT CARBOHYD 70 70 O-LINKED (GALNAC. .) (PARTIAL).  
FT CARBOHYD 72 72 O-LINKED (GALNAC. .).  
FT CARBOHYD 95 95 O-LINKED (GALNAC. .).  
FT CARBOHYD 183 183 O-LINKED (GALNAC. .).  
FT VARIANT 40 40 R -> C (IN VARIANT H).  
FT VARIANT 51 51 E -> K (IN VARIANT E).  
FT VARIANT 52 52 E -> K (IN VARIANT C).  
FT VARIANT 82 82 P -> H (IN VARIANTS A1, B, C, F AND G).  
FT VARIANT 103 103 L -> I (IN VARIANT H).  
FT VARIANT 121 121 H -> Q (IN VARIANT A3).  
FT VARIANT 132 132 E -> Q (IN VARIANTS A1 AND G).  
FT VARIANT 137 137 S -> R (IN VARIANT B).  
FT VARIANT 152 153 LP -> PL (IN VARIANTS A1 AND H).  
FT VARIANT 153 153 P -> L (IN VARIANT G).  
FT VARIANT 167 167 P -> L (IN VARIANT F).  
FT VARIANT 190 190 Q -> E (IN VARIANTS A1 AND G).  
FT VARIANT 108 108 M -> L (IN REF. 4 AND 7).  
FT CONFLICT 210 210 E -> Q (IN REF. 4 AND 7).  
FT CONFLICT 215 224 PVKPFPIIV -> DFSLLL (IN REF. 1).



SQ SEQUENCE 224 AA; 25107 MW; FOBBDD8148A238AE CRC64;  
P02666 Length: 224 February 28, 2003 14:33 Type: P Check: 8112

Initial Score = 4 Optimized Score = 4 Significance = 0.00  
Residue Identity = 80% Matches = 4 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIH  
||||  
AQTSLVYFFPGPIPNLSLPQNIPPL  
70 80 X 90

15. US-09-095-639A-1 (1-5)  
W31294 Bovine beta casein immunogenic peptide motif 2.

ID W31294 standard; peptide; 4 AA.

DE W31294;  
05-MAR-1998 (first entry)  
KW Bovine beta casein immunogenic peptide motif 2.  
KW Beta-casein; immunogenic; molecular mimicry; cow;  
OS milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
PN WO9724371-A1.  
PD 10-JUL-1997.

PF 27-DEC-1996; E05846.  
PR 27-DEC-1995; IT-RM0850.

PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
PI Pozzilli P;  
DR WPI; 97-363622/33.

PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
PS Claim 10; Page 6; 34pp; English.

CC This sequence represents an immunogenic peptide motif found in bovine  
CC beta casein. This motif is capable of mimicking a fragment of the  
CC GLUT2 protein found in insulin producing cells of the pancreas. There is  
CC a known correlation between exposure to cow's milk and the development of  
CC insulin-dependent diabetes which could possibly be linked to this  
CC molecular mimicry. Dietary or pharmaceutical products derived from milk  
CC substantially free of non-human beta casein or containing modified  
CC beta-casein without this motif could be used in diets for the prevention  
CC of insulin dependent diabetes particularly during early infancy.

SQ Sequence 4 AA;  
0 A; 0 R; 0 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 0 H;  
1 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 3 Optimized Score = 3 Significance = -1.11  
Residue Identity = 75% Matches = 3 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIH  
|||  
GPIP  
X X

16. US-09-095-639A-1 (1-5)  
aaw31294 Bovine beta casein immunogenic peptide motif 2.

TOIG of: aaw31294 check: 770 from: 1 to: 4

ID AAW31294 standard; peptide; 4 AA.  
XX  
AC AAW31294;  
XX

DT 05-MAR-1998 (first entry)  
XX

DE Bovine beta casein immunogenic peptide motif 2.

XX Beta-casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
XX Bos taurus.

OS WO9724371-A1.

PN 10-JUL-1997.

PD 27-DEC-1996; 96WO-EP05846.

PF 27-DEC-1995; 95IT-ORM0850.

PR (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

PA (MIDI-) MIDIA LTD.

PI Pozzilli P; \

DR WPI; 1997-363622/33.

PT Beta-casein or fragments not showing mimicry with GLUT2 - used in

PT food or pharmaceutical products for prevention of insulin dependent

PT diabetes, particularly in early infancy

PS Claim 10; Page 6; 34pp; English.

XX This sequence represents an immunogenic peptide motif found in bovine

XX beta casein. This motif is capable of mimicking a fragment of the

XX GLUT2 protein found in insulin producing cells of the pancreas. There is

XX a known correlation between exposure to cow's milk and the development of

XX insulin-dependent diabetes which could possibly be linked to this

XX molecular mimicry. Dietary or pharmaceutical products derived from milk

XX substantially free of non-human beta casein or containing modified

XX beta-casein without this motif could be used in diets for the prevention

XX of insulin dependent diabetes particularly during early infancy.

XX Sequence 4 AA;

AAW31294 Length: 4 March 3, 2003 11:28 Type: P Check: 770

Initial Score = 3 Optimized Score = 3 Significance = -1.11

Residue Identity = 75% Matches = 3 Mismatches = 1

Gaps = 0 Conservative Substitutions = 0

X X  
PGPIH  
|||  
GPIP  
X X

17. US-09-095-639A-1 (1-5)

p02662 Alpha-S1 casein precursor.

TOIG of: p02662 check: 2471 from: 1 to: 214

ID CAS1\_BOVIN

AC P02662; Q28048; STANDARD; PRT; 214 AA.

DT 21-JUL-1986 (Rel. 01, Created)

DT 01-NOV-1990 (Rel. 16, Last sequence update)

DT 01-MAR-2002 (Rel. 41, Last annotation update)

DE Alpha-S1 casein precursor.

GN CSN151.

OS Bos taurus (Bovine).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;

OC Bovidae; Bovinae; Bos.

OX NCBI\_taxID=9913;

RN [1]

RP SEQUENCE FROM N.A.

XX MEDLINE=84221403; PubMed=6328443;

RA Stewart A.F., Willis I.M., Mackinlay A.G.;  
 RT "Nucleotide sequences of bovine alpha S1- and kappa-casein cDNAs."  
 RL Nucleic Acids Res. 12:3895-3907(1984).  
 RN [2]  
 RP SEQUENCE FROM N.A.  
 RA Nagao M., Maki M., Sasaki R., Chiba R.;  
 RT "Isolation and sequence analysis of bovine alpha-s1-casein cDNA  
 RL clone." Biol. Chem. 48:1663-1667(1984).  
 RN [3]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=87049835; PubMed=3022833;  
 RA Gorodetskii S.I., Zakhar'ev V.M., Kyarshulite D.R., Kapelinskaya T.V.,  
 RA Skryabin K.G.;  
 RT "cDNA of cattle alpha S1-casein: cloning and nucleotide sequence."  
 RL Biochimica 51:1641-1648(1986).  
 RN [4]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=92051301; PubMed=1658736;  
 RA Koczan D., Hobom G., Seyfert H.M.;  
 RT "Genomic organization of the bovine alpha-S1 casein gene."  
 RL Nucleic Acids Res. 19:5591-5596(1991).  
 RN [5]  
 RP SEQUENCE OF 55-130 FROM N.A.  
 RX MEDLINE=83182023; PubMed=6897774;  
 RA Willis I.M., Stewart A.F., Caputo A., Thompson A.R., McKinlay A.G.;  
 RT "Construction and identification by partial nucleotide sequence  
 RL analysis of bovine casein and beta-lactoglobulin cDNA clones."  
 RN DNA 1:375-386(1982).  
 RN [6]  
 RP SEQUENCE OF 122-214 FROM N.A.  
 RX MEDLINE=85178933; PubMed=3638718;  
 RA Kyarshulite D.R., Zakhar'ev V.M., Gorodetskii S.I.;  
 RT "Nucleotide sequence of the 3'-nontranslated region of the mRNA of  
 RL alpha S1-casein in cows."  
 RN Dokl. Akad. Nauk SSSR 280:1433-1437(1985).  
 RN [7]  
 RP SEQUENCE OF 164-214 FROM N.A.  
 RX MEDLINE=94154134; PubMed=1343827;  
 RA Chen R., Wang B., Zhang Y., Liu W., Zhang J., Lao W.;  
 RT "Cloning, mapping, and sequencing of 3' and its flanking region of  
 RL bovine alpha-s1 casein gene."  
 RN Chin. J. Biotechnol. 8:235-245(1992).  
 RN [8]  
 RP SEQUENCE OF 16-214 (VARIANT B).  
 RX MEDLINE=72063417; PubMed=4331376;  
 RA Mercier J.-C., Grosclaude F., Ribadeau-Dumas B.;  
 RT "Primary structure of bovine alpha-s1 casein. Complete sequence."  
 RL Eur. J. Biochem. 23:41-51(1971).  
 RN [9]  
 RP REVISIONS TO 74 AND 92-93 (VARIANTS A; B; C AND D).  
 RX MEDLINE=74082545; PubMed=4797901;  
 RA Mercier J.-C., Grosclaude F., Ribadeau-Dumas B.;  
 RT "Primary structure of alpha casein and of bovine beta casein.  
 RL Correction." Eur. J. Biochem. 40:323-323(1973).  
 RN [10]  
 RP SEQUENCE (VARIANT D).  
 RX MEDLINE=72214259; PubMed=5064450;  
 RA Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;  
 RT "Characterization of genetic variants of alpha-s1 and beta bovine  
 RL caseins." Eur. J. Biochem. 26:328-337(1972).  
 RN [11]  
 RP SEQUENCE OF 23-49 (VARIANT A).  
 RA Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;  
 RT "Localization in the N-terminal part of bovine casein alpha-s1 of a  
 RL 13 amino-acid deletion that differentiates variant A from variants B  
 RN and C." FEBS Lett. 11:109-112(1970).  
 RN [12]  
 RP SEQUENCE OF 205-214 (VARIANT C).  
 RA Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.;

RT alpha-s1 of a Glu/Gly substitution that differentiates the genetic  
 variants B and C."  
 RL C. R. Acad. Sci., D, Sci. Nat. 268:3133-3136(1970).  
 RN [13]  
 RP REVISION (VARIANT C).  
 RA Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.;  
 RL C. R. Acad. Sci., D, Sci. Nat. 271:563-563(1970).  
 CC -1- FUNCTION: IMPORTANT ROLE IN THE CAPACITY OF MILK TO TRANSPORT  
 CC CALCIUM PHOSPHATE.  
 CC -1- SUBCELLULAR LOCATION: Extracellular.  
 CC -1- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.  
 CC -1- MISCELLANEOUS: THE B VARIANT SEQUENCE IS SHOWN.  
 CC -1- SIMILARITY: BELONGS TO THE ALPHA-CASEIN FAMILY.  
 CC -1- DATABASE: NAME=Washington enzyme manual;  
 CC WWW="http://www.washington-biochem.com/manual/C/CASA.html".  
 CC -1- DATABASE: NAME=protein Spotlight;  
 CC NOTE=Issue 16 of November 2001;  
 CC WWW="http://www.expasy.org/spotlight/articles/sptlt016.html".

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 -----

DR	EMBL; X00564; CAB57792.1; -	16	214	ALPHA-S1 CASEIN.
DR	EMBL; M33123; AAA30428.1; -	61	61	PHOSPHORYLATION.
DR	EMBL; M38641; AAA30429.1; -	63	63	PHOSPHORYLATION.
DR	EMBL; X59856; CAA42516.1; -	68	68	PHOSPHORYLATION (IN VARIANT D).
DR	EMBL; K01084; AAA30478.1; -	79	79	PHOSPHORYLATION.
DR	EMBL; M38658; AAA62707.1; -	81	81	PHOSPHORYLATION.
DR	EMBL; S72388; AAD14099.1; -	82	82	PHOSPHORYLATION.
DR	PIR; A03106; KABOSB.	83	83	PHOSPHORYLATION.
DR	PIR; A23071; A23071.	90	90	PHOSPHORYLATION.
DR	PIR; S02202; S02202.	130	130	PHOSPHORYLATION.
DR	PIR; S22575; S22575.	130	130	PHOSPHORYLATION.
DR	InterPro: IPR001588; Casein.	125	140	MISSING (IN VARIANT A).
DR	Pfam: PF00363; caseins; 1.	29	41	A -> T (IN VARIANT D).
DR	PROSITE: PS00306; CASEIN_ALPHA_BETA; 1.	68	68	E -> G (IN VARIANT C).
KW	Milk; Phosphorylation; Signal; Repeat.	207	207	P -> L (IN REF. 3).
FT	SIGNAL 1 15	42	42	E -> Q (IN REF. 4 AND 11).
FT	CHAIN 16 214	50	50	H -> Q (IN REF. 5).
FT	MOD_RES 61 61	95	95	H -> D (IN REF. 3).
FT	MOD_RES 63 63	143	143	S -> L (IN REF. 6).
FT	MOD_RES 68 68	203	203	MP -> IS (IN REF. 3).
FT	MOD_RES 79 79	212	212	
FT	MOD_RES 81 81	214	214	
FT	MOD_RES 82 82			
FT	MOD_RES 83 83			
FT	MOD_RES 90 90			
FT	MOD_RES 130 130			
FT	MOD_RES 130 130			
FT	REPEAT 85 99			
FT	REPEAT 125 140			
FT	VARIANT 29 41			
FT	VARIANT 68 68			
FT	VARIANT 207 207			
FT	CONFLICT 42 42			
FT	CONFLICT 50 50			
FT	CONFLICT 95 95			
FT	CONFLICT 143 143			
FT	CONFLICT 203 203			
FT	CONFLICT 212 212			
FT	CONFLICT 214 214			
SQ	SEQUENCE 214 AA; 24529 MW; F066B5C8AE55828B CRC64;			

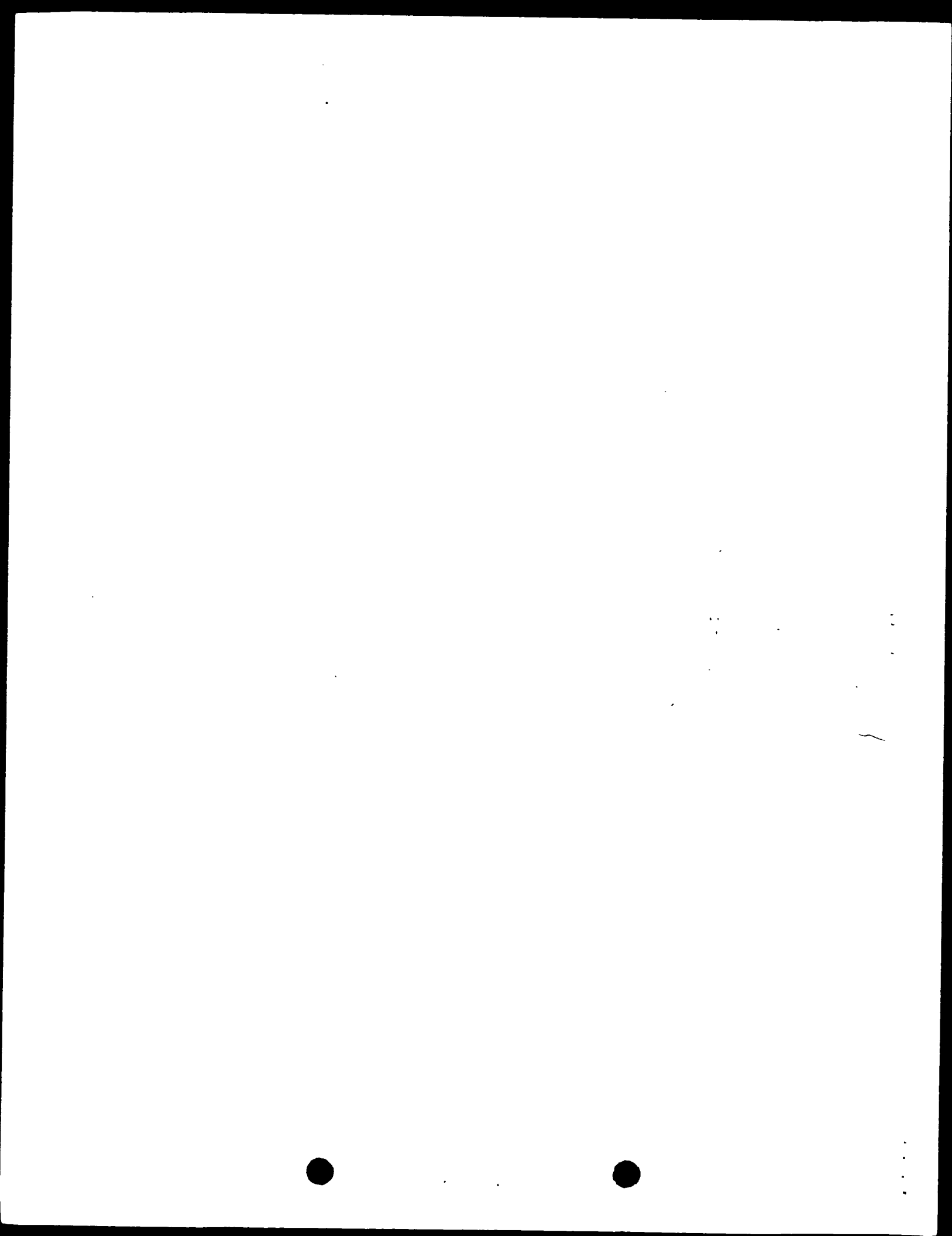
P02662 Length: 214 February 28, 2003 14:33 Type: P Check: 2471 ..

Initial Score	=	3	Optimized Score	=	4	Significance	=	-1.11
Residue Identity	=	60%	Matches	=	3	Mismatches	=	2
Gaps	=	0	Conservative Substitutions	=	0			0

X X  
PGPIH  
| |  
YTDAPSFSDIPNPIGSENSEKTMPT  
190 200 X 210

18. US-09-095-639A-1 (1-5)  
R37103 Bovine milk beta-casein enzymatic fragment.  
ID R37103 standard; peptide: 7 AA.  
AC R37103.  
DT 21-MAY-1995 (first entry)  
DE Bovine milk beta-casein enzymatic fragment.  
KW Beta-casein; enzymatic hydrolysate; cosmetics; skin disorders;  
KW wrinkles.  
OS Bos Taurus.  
PN J06166615-A.  
PD 14-JUN-1994.  
01-DEC-1992; 321624.  
01-DEC-1992; JP-321624.  
(POKK ) POLA CHEM IND INC.  
WPI; 94-230615/28.  
DR Cosmetics for treating skin disorders and wrinkles - containing  
PT enzymatic hydrolysate of human or bovine milk beta-casein  
PS Claim 2; Page 2; 7pp; Japanese.  
CC The invention relates to cosmetics containing human or bovine milk  
CC beta-casein enzymatic hydrolysate. The cosmetics are used for  
CC improving skin disorders and/or wrinkles. They are more effective  
CC than previously used polysaccharides, sugar alcohols, glycerol,  
CC glycols, etc.  
CC The present sequence is one component of the bovine milk beta-casein  
CC enzymatic hydrolysate.  
SQ Sequence 7 AA:  
SQ 1 A; 1 R; 0 N; 0 D; 0 B; 0 C; 1 Q; 0 E; 0 Z; 0 G; 0 H;  
SQ 0 I; 0 L; 0 K; 0 M; 0 P; 2 S; 0 T; 0 W; 1 Y; 1 V;  
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:04-PST using FindSeq  
Initial Score = 2 Optimized Score = 3 Significance = -2.22  
Residue Identity = 40% Matches = 2 Mismatches = 3  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIH  
| |  
AVPYQOR  
X X





Initial Score = 5 Optimized Score = 5 Significance = 1.19  
 Residue Identity = 100% Matches = 5 Mismatches = 0  
 Gaps = 0 Conservative Substitutions = 0

X X  
 PGPIP  
 |||||  
 PGPIP  
 X X

2. US-09-095-639A-2 (1-5)  
 aaw31288 Bovine beta casein variant A2 immunogenic peptide

TOIG of: aaw31288 check: 1154 from: 1 to: 5

ID AAW31288 standard; peptide; 5 AA.

AC AAW31288;

DT 05-MAR-1998 (first entry)

Bovine beta casein variant A2 immunogenic peptide motif.  
 A2 variant beta-casein; immunogenic; molecular mimicry; cow;  
 milk product; insulin-dependent diabetes; GLUT2; diet.

OS Bos taurus.  
 OS Bos indicus

PN W09724371-A1.

XX 10-JUL-1997.

PD 27-DEC-1996; 96WO-EF05846.

PF 27-DEC-1995; 95IT-ORM0850.

PR (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

XX (MIDI-) MIDIA LTD.

XX Pozzilli P;

XX WPI; 1997-363622/33.

XX Beta-casein or fragments not showing mimicry with GLUT2 - used in

XX food or pharmaceutical products for prevention of insulin dependent

XX diabetes, particularly in early infancy

XX Claim 5; Page 4; 34pp; English.

XX This sequence represents an immunogenic peptide motif from the A2 variant

XX beta-casein found in both Bos taurus and Bos indicus (amino acid

XX position 63-68). This motif is capable of mimicking a fragment of the

XX GLUT2 protein found in insulin producing cells of the pancreas. There is

XX a known correlation between exposure to cow's milk and the development of

XX insulin-dependent diabetes which could possibly be linked to this

XX molecular mimicry. Dietary or pharmaceutical products derived from milk

XX substantially free of non-human beta casein or containing modified

XX beta-casein without this motif could be used in diets for the prevention

XX of insulin dependent diabetes particularly during early infancy.

XX Sequence 5 AA;

XX AAW31288 Length: 5 March 3, 2003 11:28 Type: P Check: 1154

XX Initial Score = 5 Optimized Score = 5 Significance = 1.19

XX Residue Identity = 100% Matches = 5 Mismatches = 0

XX Gaps = 0 Conservative Substitutions = 0

XX X X

XX PGPIP

XX |||||

XX

XX

XX

XX

XX

XX

XX

XX

PGPIP  
 X X

3. US-09-095-639A-2 (1-5)  
 p02666 Beta casein precursor.

TOIG of: p02666 check: 8112 from: 1 to: 224

ID CASE\_BOVIN STANDARD; PRT; 224 AA.

DT 21-JUL-1986 (Rel. 01, Created)

DT 01-MAR-1989 (Rel. 10, Last sequence update)

DT 01-MAR-2002 (Rel. 41, Last annotation update)

DE Beta casein precursor.

GN CSN2.

OS Bos taurus (Bovine).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;

OC Bovidae; Bovinae; Bos.

OX NCBI\_TaxID=9913;

RN . [1]

RP SEQUENCE FROM N.A.

RA Baev A.A., Smirnov I.K., Gorodetsky S.I.;

RT "Primary structure of bovine beta-casein cDNA.;"

RL Mol. Biol. (Mosk) 21:214-222(1987).

RN [2]

RP SEQUENCE FROM N.A.

RA MEDLINE=8818899; PubMed=2833669;

RT Stewart A.F., Bonsing J., Beattie C.W., Shah F., Willis I.M.,

RL Mackinlay A.G.;

RT "Complete nucleotide sequences of bovine alpha S2- and beta-casein

CDNAs: comparisons with related sequences in other species.;"

RL Mol. Biol. Evol. 4:231-241(1987).

RN [3]

RP SEQUENCE FROM N.A.

RA MEDLINE=90147279; PubMed=3271384;

RT Bonsing J., Ring J.M., Stewart A.F., Mackinlay A.G.;

RL "Complete nucleotide sequence of the bovine beta-casein gene.;"

RN Aust. J. Biol. Sci. 41:527-537(1988).

RP SEQUENCE FROM N.A.

RA MEDLINE=87128158; PubMed=3814153;

RT Jimenez-Flores R., Kang Y.C., Richardson T.;

RL "Cloning and sequence analysis of bovine beta-casein cDNA.;"

RN Biochem. Biophys. Res. Commun. 142:617-621(1987).

RP SEQUENCE FROM N.A. (VARIANT A3).

RC TISSUE=Mammary gland;

RX MEDLINE=94068382; PubMed=8248100;

RA Simons G., van den Heuvel W., Reynen T., Frijters A., Rutten G.,

RT Slangen C.J., Groenen M., de Vos W.M., Siezen R.J.;

RL "Overproduction of bovine beta-casein in Escherichia coli and

engineering of its main chymosin cleavage site.;"

RN protein Eng. 6:763-770(1993).

RP SEQUENCE OF 16-224 (VARIANT A2).

RX MEDLINE=88152252; PubMed=3278933;

RT Carles C., Huet J.-C., Ribadeau-Dumas B.;

RL "A new strategy for primary structure determination of proteins:

application to bovine beta-casein.;"

RN FEBS Lett. 229:265-272(1988).

RP SEQUENCE OF 16-224 (VARIANT A2).

RX MEDLINE=72233212; PubMed=4557764;

RA Ribadeau-Dumas B., Brignon G., Grosclaude F., Mercier J.-C.;

RT "Primary structure of bovine beta casein. Complete sequence.;"

RN Eur. J. Biochem. 25:505-514(1972).

RP VARIANTS A1; B AND C.

RX MEDLINE=72214259; PubMed=5064450;

RA Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;

RT "Characterization of genetic variants of alpha-S1 and beta bovine

RT RT caseins.";  
RN Eur. J. Biochem. 26:328-337(1972).  
RP [9]  
RX SEQUENCE OF 118-124 (VARIANT A3).  
RA MEDLINE=71252171; PubMed=4997616;  
RA Ribadeau-Dumas B., Grosclaude F., Mercier J.-C.;  
RT "Localization in the peptide chain of bovine beta casein of the  
RT His-Gln substitution differentiating the A2 and A3 genetic  
RT variants.";  
RN C. R. Acad. Sci., D, Sci. Nat. 270:2369-2372(1970).  
RN [10]  
RP SEQUENCE OF 48-63 (VARIANT E).  
RX MEDLINE=75005247; PubMed=4411121;  
RA Grosclaude F., Mahe M.-F., Voglino G.-F.;  
RT "The beta E variant and the phosphorylation code of bovine caseins.";  
RN FEBS Lett. 45:3-5(1974).  
RN [11]  
RP SEQUENCE OF 68-105 FROM N.A.  
RX MEDLINE=85155504; PubMed=6397405;  
RA Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,  
RT Sulimova G.E., Judinkova E.S., Gorodetsky S.I.;  
RT "Identification of bacterial clones encoding bovine caseins by direct  
RT immunological screening of the cDNA library.";  
RN Gene 32:381-388(1984).  
RN [12]  
RP SEQUENCE OF 68-95 FROM N.A.  
RX MEDLINE=86014005; PubMed=3900695;  
RA Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,  
RA Sulimova G.E.;  
RT "Identification of bacterial clones coding for bovine caseins by  
RT direct immunologic screening of the cDNA library.";  
RN Mol. Biol. (Mosk) 19:955-963(1985).  
RN [13]  
RP SEQUENCE OF 18-57 FROM N.A., AND SEQUENCE OF 16-224 (VARIANT H).  
RX MEDLINE=20154951; PubMed=10690361;  
RA Han S.K., Shin Y.C., Byun H.D.;  
RT "Biochemical, molecular and physiological characterization of a new  
RT beta-casein variant detected in Korean cattle.";  
RN Anim. Genet. 31:49-51(2000).  
RN [14]  
RP SEQUENCE OF 125-195 (VARIANTS A1 AND G).  
RA Dong C., Ng-Kwai-Hang K.F.;  
RT "Characterization of a non-electrophoretic genetic variant of beta-  
RT casein by peptide mapping and mass spectrometric analysis.";  
RN Int. Dairy J. 8:967-972(1998).  
RN [15]  
RP SEQUENCE OF 160-171 (VARIANT F).  
RX MEDLINE=96118672; PubMed=7496485;  
RA Visser S., Slangen C.J., Lagerwerf F.M., Van Dongen W.D.,  
RA Haverkamp J.;  
RT "Identification of a new genetic variant of bovine beta-casein using  
RT reversed-phase high-performance liquid chromatography and mass  
RT spectrometric analysis.";  
RN J. Chromatogr. A 711:141-150(1995).  
RN [16]  
RP SEQUENCE OF 170-184 FROM N.A.  
RX MEDLINE=83182023; PubMed=6897774;  
RA Willis I.M., Stewart A.F., Caputo A., Thompson A.R., McKinlay A.G.;  
RT "Construction and identification by partial nucleotide sequence  
RT analysis of bovine casein and beta-lactoglobulin cDNA clones.";  
RN DNA 1:375-386(1982).  
RN [17]  
RP CARBOHYDRATE-LINKAGE SITES.  
RX MEDLINE=85000478; PubMed=6148101;  
RA Yan S.B., Wold F.;  
RT "Neoglycoproteins: in vitro introduction of glycosyl units at  
RT glutamines in beta-casein using transglutaminase.";  
RN Biochemistry 23:3759-3765(1984).  
CC -1- FUNCTION: IMPORTANT ROLE IN DETERMINATION OF THE SURFACE  
CC PROPERTIES OF THE CASEIN MICELLES.  
CC -1- SUBCELLULAR LOCATION: Extracellular.  
CC -1- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.  
CC -1- POLYMORPHISM: LEU-152 IS PRESENT IN THE VARIANTS F AND G; GLN-190

CC AND GLU-210 ARE PRESENT IN THE VARIANT H. THE SEQUENCE SHOWN IS  
CC THE A2 VARIANT.  
CC -1- SIMILARITY: BELONGS TO THE BETA-CASEIN FAMILY.  
CC -1- DATABASE: NAME-Protein Spotlight;  
CC NOTE-Issue 16 of November 2001;  
CC WWW="http://www.expasy.org/spotlight/articles/sptl016.html".  
CC -----  
CC This SWISS-PROT entry is copyright. It is produced through a collaboration  
CC between the Swiss Institute of Bioinformatics and the EMBL outstation -  
CC the European Bioinformatics Institute. There are no restrictions on its  
CC use by non-profit institutions as long as its content is in no way  
CC modified and this statement is not removed. Usage by and for commercial  
CC entities requires a license agreement (See http://www.isb-sib.ch/announce/  
CC or send an email to license@isb-sib.ch).  
CC -----  
DR EMBL; M16645; AAA30480.1; -  
DR EMBL; M15132; AAA30430.1; -  
DR EMBL; K01087; AAA30481.1; -  
DR EMBL; X06359; CAA29658.1; -  
DR EMBL; M55158; AAA30431.1; -  
DR EMBL; S67277; AAB29137.1; -  
DR EMBL; AF104929; AAD09813.1; -  
DR EMBL; AF104928; AAD09813.1; JOINED.  
DR EMBL; M64756; AAB59254.1; -  
DR PIR; A03110; KBOA2.  
DR PIR; A25846; A25846.  
DR PIR; B29087; B29087.  
DR PIR; S01860; S01860.  
DR PIR; S02429; S02429.  
DR CarDbank; CCSD:9067; -  
DR InterPro; IPR001588; Casein.  
DR Pfam; PF00363; caseins; 1.  
DR PROSITE; PS00306; CASEIN\_ALPHA\_BETA; 1.  
KW Milk; Phosphorylation; Glycoprotein; Signal; Polymorphism.  
FT SIGNAL 1 15  
FT CHAIN 16 224  
FT MOD\_RES 30 30 BETA CASEIN.  
FT MOD\_RES 32 32 PHOSPHORYLATION.  
FT MOD\_RES 33 33 PHOSPHORYLATION.  
FT MOD\_RES 34 34 PHOSPHORYLATION.  
FT MOD\_RES 50 50 PHOSPHORYLATION (EXCEPT IN VARIANT C).  
FT CARBOHYD 70 72 O-LINKED (GALNAc. . .) (PARTIAL).  
FT CARBOHYD 72 72 O-LINKED (GALNAc. . .).  
FT CARBOHYD 95 95 O-LINKED (GALNAc. . .).  
FT CARBOHYD 183 183 O-LINKED (GALNAc. . .).  
FT VARIANT 40 40 R -> C (IN VARIANT H).  
FT VARIANT 51 51 E -> K (IN VARIANT E).  
FT VARIANT 52 52 E -> K (IN VARIANT C).  
FT VARIANT 82 82 P -> H (IN VARIANTS A1, B, C, F AND G).  
FT VARIANT 103 103 L -> I (IN VARIANT H).  
FT VARIANT 121 121 H -> Q (IN VARIANT A3).  
FT VARIANT 132 132 E -> Q (IN VARIANTS A1 AND G).  
FT VARIANT 137 137 S -> R (IN VARIANT B).  
FT VARIANT 152 153 LP -> PL (IN VARIANTS A1 AND H).  
FT VARIANT 153 153 P -> L (IN VARIANT G).  
FT VARIANT 167 167 P -> L (IN VARIANT F).  
FT VARIANT 190 190 Q -> E (IN VARIANTS A1 AND G).  
FT CONFLICT 108 108 M -> L (IN REF. 4 AND 7).  
FT CONFLICT 210 210 E -> Q (IN REF. 4 AND 7).  
FT CONFLICT 215 224 PVRGPPPIIV -> DPSLLL (IN REF. 1).  
SQ SEQUENCE 224 AA; 25107 MW; F0BDD8148A238AE CRC64;  
P02666 Length: 224 February 28, 2003 14:33 Type: P Check: 8112 ..  
Initial Score = 5 Optimized Score = 5 Significance = 1.19  
Residue Identity = 100% Matches = 5 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0  
X X  
PGPIP  
|||||  
AQTQSLVYPPFGPIPNLSLPQNPPL  
70 80 X 90





CC a known correlation between exposure to cow's milk and the development of  
 CC insulin-dependent diabetes which could possibly be linked to this  
 CC molecular mimicry. Dietary or pharmaceutical products derived from milk  
 CC substantially free of non-human beta casein or containing modified  
 CC beta-casein without this motif could be used in diets for the prevention  
 CC of insulin dependent diabetes particularly during early infancy.  
 SQ Sequence 4 AA;  
 SQ 0 A; 0 R; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 0 H;  
 SQ 1 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
 CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 4 Optimized Score = 4 Significance = 0.00  
 Residue Identity = 100% Matches = 4 Mismatches = 0  
 Gaps = 0 Conservative Substitutions = 0

X X  
 PGPPI  
 I I I I  
 GPIP  
 X X

7. US-09-095-639A-2 (1-5)  
 aaw31294 Bovine beta casein immunogenic peptide motif 2.

TOIG of: aaw31294 check: 770 from: 1 to: 4

ID AAW31294 standard; peptide; 4 AA.  
 XX AAW31294;  
 AC AAW31294;  
 XX AAW31294;

05-MAR-1998 (first entry)

Bovine beta casein immunogenic peptide motif 2.

Beta-casein; immunogenic; molecular mimicry; cow;  
 milk product; insulin-dependent diabetes; GLUT2; diet.

Bos taurus.

WO9724371-A1.

10-JUL-1997.

27-DEC-1996; 96WO-EP05846.

27-DEC-1995; 95IT-OR0850.

(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
 (MIDI-) MIDIA LTD.

Pozzilli P;

WPI; 1997-363622/33.

Beta-casein or fragments not showing mimicry with GLUT2 - used in  
 food or pharmaceutical products for prevention of insulin dependent  
 diabetes, particularly in early infancy

Claim 10; Page 6; 34pp; English.

This sequence represents an immunogenic peptide motif found in bovine  
 beta casein. This motif is capable of mimicking a fragment of the  
 GLUT2 protein found in insulin producing cells of the pancreas. There is  
 a known correlation between exposure to cow's milk and the development of  
 insulin-dependent diabetes which could possibly be linked to this  
 molecular mimicry. Dietary or pharmaceutical products derived from milk  
 substantially free of non-human beta casein or containing modified  
 beta-casein without this motif could be used in diets for the prevention  
 of insulin dependent diabetes particularly during early infancy.

Sequence 4 AA;

SQ

AAW31294 Length: 4 March 3, 2003 11:28 Type: P Check: 770 ..  
 Initial Score = 4 Optimized Score = 4 Significance = 0.00  
 Residue Identity = 100% Matches = 4 Mismatches = 0  
 Gaps = 0 Conservative Substitutions = 0

X X  
 PGPPI  
 I I I I  
 GPIP  
 X X

8. US-09-095-639A-2 (1-5)  
 W31287 Bovine beta casein variant A1 immunogenic peptide

ID W31287 standard; peptide; 5 AA.

AC W31287;

05-MAR-1998 (first entry)

Bovine beta casein variant A1 immunogenic peptide motif.

Al variant beta casein; immunogenic; molecular mimicry; cow;  
 milk product; insulin-dependent diabetes; GLUT2; diet.

Bos taurus.

WO9724371-A1.

10-JUL-1997.

27-DEC-1996; E05846.

27-DEC-1995; IT-OR0850.

(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

(MIDI-) MIDIA LTD.

Pozzilli P;

WPI; 97-363622/33.

Beta-casein or fragments not showing mimicry with GLUT2 - used in  
 food or pharmaceutical products for prevention of insulin dependent  
 diabetes, particularly in early infancy

Claim 5; Page 3; 34pp; English.

This sequence represents an immunogenic peptide motif from the A1  
 variant of beta-casein which is capable of mimicking a fragment of the  
 GLUT2 protein found in insulin producing cells of the pancreas. There is  
 a known correlation between exposure to cow's milk and the development of  
 insulin-dependent diabetes which could possibly be linked to this  
 molecular mimicry. Dietary or pharmaceutical products derived from milk  
 substantially free of non-human beta casein or containing modified  
 beta-casein without this motif could be used in diets for the prevention  
 of insulin dependent diabetes particularly during early infancy.

Sequence 5 AA;

SQ 0 A; 0 R; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 1 H;  
 SQ 1 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
 CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 4 Optimized Score = 4 Significance = 0.00  
 Residue Identity = 80% Matches = 4 Mismatches = 1  
 Gaps = 0 Conservative Substitutions = 0

X X  
 PGPPI  
 I I I I  
 GPIP  
 X X

9. US-09-095-639A-2 (1-5)  
 aaw31287 Bovine beta casein variant A1 immunogenic peptide

TOIG of: aaw31287 check: 1114 from: 1 to: 5

ID AAW31287 standard; peptide; 5 AA.

XX AAW31287;

AC AAW31287;

05-MAR-1998 (first entry)

Bovine beta casein variant A1 immunogenic peptide motif.

XX

CC This sequence represents an immunogenic peptide from the A1 variant of  
CC beta-casein which contains a motif (see W31287) capable of mimicking a  
CC fragment of the GLUT2 protein found in insulin producing cells of the  
CC pancreas. There is a known correlation between exposure to cow's milk and  
CC the development of insulin-dependent diabetes which could possibly be  
CC linked to this molecular mimicry. Dietary or pharmaceutical products  
CC derived from milk substantially free of non-human beta casein or  
CC containing modified beta-casein without this motif could be used in diets  
CC for the prevention of insulin dependent diabetes particularly during  
CC early infancy.  
SQ Sequence 12 AA;  
SQ 0 A; 0 R; 1 N; 0 D; 0 B; 0 C; 0 O; 0 E; 0 Z; 1 G; 1 H;  
SQ 1 I; 1 L; 0 K; 0 M; 1 F; 3 P; 1 S; 0 T; 0 W; 1 Y; 1 V;  
CC Retrieved by bobryon on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 4 Optimized Score = 4 Significance = 0.00  
Residue Identity = 80% Matches = 4 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X X  
X  
PGPIP  
||||  
SLVYPPFGPIHN  
X 10

11. US-09-095-639A-2 (1-5)  
aaw31289 Bovine beta casein variant A1 immunogenic peptide.

TOIG of: aaw31289 check: 5975 from: 1 to: 12

ID AAW31289 standard; peptide; 12 AA.  
XX  
AC AAW31289;  
XX  
DT .05-MAR-1998 (first entry)  
XX  
DE Bovine beta casein variant A1 immunogenic peptide.  
XX  
KW Al variant beta casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
XX  
PN WO9724371-A1.  
XX  
PD 10-JUL-1997.  
XX  
PF 27-DEC-1996; 96WO-EP05846.  
XX  
PR 27-DEC-1995; 95IT-ORM0850.  
XX  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
XX  
PI Pozzilli P;  
XX  
DR WPI; 1997-363622/33.  
XX  
PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
XX  
PS Claim 5; Page 3; 34pp; English.  
XX  
CC This sequence represents an immunogenic peptide from the A1 variant of  
CC beta-casein which contains a motif (see AAW31287) capable of mimicking a  
CC fragment of the GLUT2 protein found in insulin producing cells of the  
CC pancreas. There is a known correlation between exposure to cow's milk  
CC and the development of insulin-dependent diabetes which could possibly  
CC be linked to this molecular mimicry. Dietary or pharmaceutical products  
CC derived from milk substantially free of non-human beta casein or  
CC containing modified beta-casein without this motif could be used in  
CC diets containing modified beta-casein without this motif could be used in

Al variant beta casein; immunogenic; molecular mimicry; cow;  
milk product; insulin-dependent diabetes; GLUT2; diet.  
Bos taurus.  
WO9724371-A1.  
10-JUL-1997.  
27-DEC-1996; 96WO-EP05846.  
27-DEC-1995; 95IT-ORM0850.  
(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
(MIDI-) MIDIA LTD.  
Pozzilli P;  
WPI; 1997-363622/33.  
Beta-casein or fragments not showing mimicry with GLUT2 - used in  
food or pharmaceutical products for prevention of insulin dependent  
diabetes, particularly in early infancy  
Claim 5; Page 3; 34pp; English.  
This sequence represents an immunogenic peptide motif from the A1  
variant of beta-casein which is capable of mimicking a fragment of the  
GLUT2 protein found in insulin producing cells of the pancreas. There is  
a known correlation between exposure to cow's milk and the development of  
insulin-dependent diabetes which could possibly be linked to this  
molecular mimicry. Dietary or pharmaceutical products derived from milk  
substantially free of non-human beta casein or containing modified  
beta-casein without this motif could be used in diets for the prevention  
of insulin dependent diabetes particularly during early infancy.

Sequence 5 AA;  
AAW31287 Length: 5 March 3, 2003 11:29 Type: P Check: 1114 ..  
Initial Score = 4 Optimized Score = 4 Significance = 0.00  
Residue Identity = 80% Matches = 4 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X X  
X  
PGPIP  
||||  
PGPIH  
X X

10. US-09-095-639A-2 (1-5)  
W31289 Bovine beta casein variant A1 immunogenic peptide.

ID W31289 standard; peptide; 12 AA.  
AC W31289;  
DT 05-MAR-1998 (first entry)  
DE Bovine beta casein variant A1 immunogenic peptide.  
KW Al variant beta casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
XX  
PN WO9724371-A1.  
XX  
PD 10-JUL-1997.  
XX  
PF 27-DEC-1996; E05846.  
XX  
PR 27-DEC-1995; IT-RM0850.  
XX  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
XX  
PI Pozzilli P;  
XX  
DR WPI; 97-363622/33.  
XX  
PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
XX  
PS Claim 5; Page 3; 34pp; English.

CC diets for the prevention of insulin dependent diabetes particularly  
 CC during early infancy.  
 XX  
 SQ Sequence 12 AA;

AAW31289 Length: 12 March 3, 2003 11:28 Type: P Check: 5975  
 Initial Score = 4 Optimized Score = 4 Significance = 0.00  
 Residue Identity = 80% Matches = 4 Mismatches = 1  
 Gaps = 0 Conservative Substitutions = 0

X X  
 PGPIP  
 ||||  
 SLVYPPGPIHN  
 X 10

US-09-095-639a-2 (1-5)  
 R95609 Bovine beta casein A1 variant.

ID R95609 standard; protein; 209 AA.  
 AC R95609;  
 DT 26-NOV-1996 (first entry)  
 DE Bovine beta casein A1 variant.  
 KW Milk; beta casein; diabetogenic; diabetes; cow; milk products;  
 OS butter; cheese; cream.  
 FH Bos taurus.  
 Key Location/Qualifiers  
 FT region 63..68  
 PN /label= Diabetogenic hexapeptide.  
 PD W09614577-A1.  
 PF 17-MAY-1996.  
 PR 03-NOV-1995; NZ0114.  
 PA 04-NOV-1994; NZ-264862.  
 PA (NACH-) NAT CHILD HEALTH RES FOUND.  
 PA (NZDA-) NEW ZEALAND DAIRY BOARD.  
 PI Elliott RE, Hill JP;  
 DR WPI; 96-251885/25.  
 FT Selecting non-diabetogenic milk and milk prods. - by testing milk or  
 FT cows for the presence of non-diabetogenic variants of beta-casein  
 PS Disclosure; Figure 2; 28pp; English.  
 CC A method for selecting milk for feeding to diabetes susceptible  
 CC individuals comprises testing milk from identified cows for the  
 CC presence of variants of beta casein and selecting those cows whose  
 CC milk contains non-diabetogenic variants and milking these cows  
 CC separately. The milk and milk products obtained can reduce the risk  
 CC of susceptible individuals contracting Type-1 diabetes.  
 SQ Sequence 209 AA;  
 SQ 5 A; 4 R; 4 N; 5 D; 0 B; 0 C; 21 Q; 18 E; 0 Z; 5 G; 6 H;  
 SQ 10 I; 22 L; 11 K; 6 M; 9 F; 34 P; 16 S; 9 T; 1 W; 4 Y; 19 V;  
 CC Retrieved by bobryen on Thu 27 Feb 103 16:22:05-PST using FindSeq

Initial Score = 4 Optimized Score = 4 Significance = 0.00  
 Residue Identity = 80% Matches = 4 Mismatches = 1  
 Gaps = 0 Conservative Substitutions = 0

X X  
 PGPIP  
 ||||  
 AQTQSLVYPPGPIHNSLPQNTPL  
 60 X X 70

13. US-09-095-639a-2 (1-5)  
 R80281 Methyl or ethyl esterified bovine beta-casein A1.  
 ID R80281 standard; protein; 209 AA.  
 AC R80281;  
 DT 14-FEB-1996 (first entry)  
 DE Methyl or ethyl esterified bovine beta-casein A1.  
 KW Bovine; beta-casein; ethyl esterification; pepsin hydrolysis;  
 KW proteolysis; peptide ester; food; pharmaceutical; cosmetics.

OS	Bos taurus.	Location/Qualifiers
FT	Key	1..209
FT	protein	/note= "55% esterified by methanol or by ethanol, resulting in atypical pepsin cleavage sites, in addition to the naturally occurring (native) sites"
FT	cleavage_site	4..5
FT	cleavage_site	/note= "pepsin cleavage site in native protein"
FT	cleavage_site	5..6
FT	cleavage_site	/note= "pepsin cleavage site in native protein and in methyl ester of beta-casein"
FT	cleavage_site	11..12
FT	cleavage_site	/note= "newly identified pepsin cleavage site in methyl ester of beta-casein"
FT	cleavage_site	15..16
FT	cleavage_site	/note= "pepsin cleavage site in native protein"
FT	cleavage_site	44..45
FT	cleavage_site	/note= "pepsin cleavage site in native protein"
FT	cleavage_site	45..46
FT	cleavage_site	/note= "pepsin cleavage site in native protein and in ethyl ester of beta-casein"
FT	cleavage_site	55..56
FT	cleavage_site	/note= "pepsin cleavage site in native protein and in ethyl ester of beta-casein"
FT	cleavage_site	57..58
FT	cleavage_site	/note= "pepsin cleavage site in native protein and in ethyl ester of beta-casein"
FT	cleavage_site	58..59
FT	cleavage_site	/note= "pepsin cleavage site in native protein and in ethyl ester of beta-casein"
FT	cleavage_site	72..73
FT	cleavage_site	/note= "pepsin cleavage site in native protein"
FT	cleavage_site	73..74
FT	cleavage_site	/note= "newly identified pepsin cleavage site in methyl ester of beta-casein"
FT	cleavage_site	80..81
FT	cleavage_site	/note= "pepsin cleavage site in native protein and in ethyl ester of beta-casein"
FT	cleavage_site	93..94
FT	cleavage_site	/note= "pepsin cleavage site in native protein and in ethyl ester of beta-casein"
FT	cleavage_site	125..126
FT	cleavage_site	/note= "pepsin cleavage site in native protein"
FT	cleavage_site	126..127
FT	cleavage_site	/note= "pepsin cleavage site in native protein"
FT	cleavage_site	127..128
FT	cleavage_site	/note= "pepsin cleavage site in native protein"
FT	cleavage_site	141..142
FT	cleavage_site	/note= "pepsin cleavage site in native protein"
FT	cleavage_site	142..143
FT	cleavage_site	/note= "pepsin cleavage site in native protein and in methyl ester of beta-casein"
FT	cleavage_site	156..157
FT	cleavage_site	/note= "newly identified pepsin cleavage site in ethyl ester of beta-casein"
FT	cleavage_site	162..163
FT	cleavage_site	/note= "newly identified pepsin cleavage site in ethyl ester of beta-casein"
FT	cleavage_site	163..164
FT	cleavage_site	/note= "pepsin cleavage site in native protein and in methyl ester of beta-casein"
FT	cleavage_site	164..165
FT	cleavage_site	/note= "pepsin cleavage site in native protein and in ethyl ester of beta-casein"
FT	cleavage_site	188..189
FT	cleavage_site	/note= "pepsin cleavage site in native protein and in methyl ester of beta-casein"
FT	cleavage_site	189..190
FT	cleavage_site	/note= "pepsin cleavage site in native protein and in methyl ester of beta-casein"
FT	cleavage_site	190..191
FT	cleavage_site	/note= "pepsin cleavage site in native protein and in methyl ester of beta-casein"

FT cleavage\_site 191..192 in ethyl ester of beta-casein"

FT /note= "pepsin cleavage site in native protein and

FT in methyl and ethyl esters of beta-casein"

FT cleavage\_site 192..193

FT /note= "pepsin cleavage site in native protein and

FT in methyl and ethyl esters of beta-casein"

FT cleavage\_site 198..199

FT /note= "newly identified pepsin cleavage site in

FT methyl and ethyl esters of beta-casein"

FT cleavage\_site 207..208

FT /note= "newly identified pepsin cleavage site in

FT methyl ester of beta-casein"

FT peptide 2..25

FT /label= A

FT /note= "tryptic peptide from native protein"

FT peptide 26..28

FT /label= B

FT /note= "tryptic peptide from native protein"

FT peptide 29..32

FT /label= C

FT /note= "tryptic peptide from native protein"

FT peptide 33..48

FT /label= D

FT /note= "tryptic peptide from native protein"

FT peptide 49..97

FT /label= E

FT /note= "tryptic peptide from native protein"

FT peptide 100..105

FT /label= F

FT /note= "tryptic peptide from native protein"

FT peptide 106..107

FT /label= G

FT /note= "tryptic peptide from native protein"

FT peptide 108..113

FT /label= H

FT /note= "tryptic peptide from native protein"

FT peptide 114..169

FT /label= I

FT /note= "tryptic peptide from native protein"

FT peptide 170..176

FT /label= J

FT /note= "tryptic peptide from native protein"

FT peptide 177..183

FT /label= K

FT /note= "tryptic peptide from native protein"

FT peptide 184..202

FT /label= L

FT /note= "tryptic peptide from native protein"

FT peptide 203..209

FT /label= N

FT /note= "tryptic peptide from native protein"

FT modified\_site 15

FT /note= "phosphorylated"

FT modified\_site 17

FT /note= "phosphorylated"

FT modified\_site 18

FT /note= "phosphorylated"

FT modified\_site 19

FT /note= "phosphorylated"

FT modified\_site 35

FT /note= "phosphorylated"

PN W09517518-Al.

PD 29-JUN-1995.

PF 20-DEC-1994; F01500.

PR 23-DEC-1994; FR-015764.

PA (INRG) INST NAT RECH AGRONOMIQUE.

PI Briand L, Chobert J, Haertle T;

DR WPI; 95-240679/31.

PT New esterified amino acids, peptide(s) and their mixts. - prepd. by

PT esterification of protein then enzymatic hydrolysis, useful as

PT ingredients and additives in foods, pharmaceuticals and cosmetics

PS Claim 7; Fig 7 and 18; 47pp; French.

CC The native form of bovine beta-casein A1 contains various pepsin

CC cleavage sites. Esterification of the protein with methanol or ethanol

CC results in a form of beta-casein contg. additional, non-conventional

CC pepsin cleavage sites (see Features Table). Esterified peptides and

CC amino acids (and their mixtures) resulting from hydrolysis of an

CC esterified protein (pref. beta-lactoglobulin or beta-casein) are

CC claimed. The hydrolysis products are useful as ingredients,

CC additives or active agents in foods, pharmaceuticals and cosmetics.

SO Sequence 209 AA;

SO 5 A; 4 R; 5 N; 4 D; 0 B; 0 C; 20 Q; 19 E; 0 Z; 5 G; 6 H;

SO 10 I; 22 L; 11 K; 6 M; 9 F; 34 P; 16 S; 9 T; 1 W; 4 Y; 19 V;

CC Retrieved by Bobryen on Thu 27 Feb 103 16:22:04-PST using FindSeq

Initial Score = 4 Optimized Score = 4 Significance = 0.00

Residue Identity = 80% Matches = 4 Mismatches = 1

Gaps = 0 Conservative Substitutions = 0

X X X

GGPIP

||||

AQTQSLVYPPPPGPIHNSLPONIPPL

60 X X 70

14. US-09-095-639A-2 (1-5)

aar95609 Bovine beta casein A1 variant.

TOIG of: aar95609 check: 2014 from: 1 to: 209

ID AAR95609 standard; protein; 209 AA.

AC AAR95609;

XX

XX 26-NOV-1996 (first entry)

XX

XX Bovine beta casein A1 variant.

DE

XX Milk; beta casein; diabetogenic; diabetes; cow; milk products;

KW butter; cheese; cream.

XX

XX Bos taurus.

XX

XX Key Location/Qualifiers

FH Region 63..68

FT /label= Diabetogenic hexapeptide.

XX WO9614577-Al.

XX

XX 17-MAY-1996.

XX

XX 03-NOV-1995; 95WO-NZ00114.

XX

XX 04-NOV-1994; 94NZ-0264862.

XX

XX (NACH-) NAT CHILD HEALTH RES FOUND.

PA (NZDA-) NEW ZEALAND DAIRY BOARD.

XX

XX Elliott RB, Hill JP;

XX

XX WPI; 1996-251885/25.

XX

XX Selecting non-diabetogenic milk and milk prods. - by testing milk or

XX cows for the presence of non-diabetogenic variants of beta-casein

XX Disclosure; Figure 2; 28pp; English.

XX

XX A method for selecting milk for feeding to diabetes susceptible

XX individuals comprises testing milk from identified cows for the

XX presence of variants of beta casein and selecting those cows whose

XX milk contains non-diabetogenic variants and milking these cows

XX separately. The milk and milk products obtained can reduce the risk

XX of susceptible individuals contracting Type-1 diabetes.

SQ Sequence 209 AA;  
AAR95609 Length: 209 March 3, 2003 11:28 Type: P Check: 2014 ..  
Initial Score = 4 Optimized Score = 0.00  
Residue Identity = 80% Matches = 4 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0  
X X  
PGPIP  
||||  
AQTQSLVYPFGPIHNSLPQNIPPL  
60 X X 70  
15. US-09-095-639A-2 (1-5)  
W31293 Bovine beta casein immunogenic peptide motif 1.  
W31293 standard; peptide; 4 AA.  
W31293;  
05-MAR-1998 (first entry)  
DE Bovine beta casein immunogenic peptide motif 1.  
KW Beta casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
PN W09724371-A1.  
PD 10-JUL-1997.  
PF 27-DEC-1996; E05846.  
PR 27-DEC-1995; IT-RW0850.  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
PI Pozzilli P;  
DR WPI; 97-363622/33.  
PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
PS Claim 10; Page 6; 34pp; English.  
CC This sequence represents an immunogenic peptide motif of beta-casein  
CC which is capable of mimicking a fragment of the GLUT2 protein found in  
CC insulin producing cells of the pancreas. There is a known correlation  
CC between exposure to cow's milk and the development of insulin-dependent  
CC diabetes which could possibly be linked to this molecular mimicry.  
CC Dietary or pharmaceutical products derived from milk substantially free  
CC of non-human beta casein or containing modified beta-casein without this  
CC motif could be used in diets for the prevention of insulin dependent  
CC diabetes particularly during early infancy.  
SQ Sequence 4 AA;  
0 A; 0 R; 0 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 2; 1 G; 1 H;  
1 I; 0 L; 0 K; 0 M; 0 F; 1 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq  
Initial Score = 3 Optimized Score = 3 Significance = -1.19  
Residue Identity = 75% Matches = 3 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0  
X X  
PGPIP  
||||  
GPIH  
X X  
16. US-09-095-639A-2 (1-5)  
aaw31293 Bovine beta casein immunogenic peptide motif 1.  
TOIG of: aaw31293 check: 738 from: 1 to: 4  
ID AAW31293 standard; peptide; 4 AA.  
XX AAW31293;  
AC AAW31293;  
XX 05-MAR-1998 (first entry)  
DT 05-MAR-1998 (first entry)  
RX MEDLINE=84221403; PubMed=6328443;

DE Bovine beta casein immunogenic peptide motif 1.  
XX Beta casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
XX Bos taurus.  
XX W09724371-A1.  
XX 10-JUL-1997.  
XX 27-DEC-1996; 96WO-EP05846.  
XX 27-DEC-1995; 95IT-ORM0850.  
XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
XX (MIDI-) MIDIA LTD.  
XX Pozzilli P;  
XX WPI; 1997-363622/33.  
XX Beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
XX Claim 10; Page 6; 34pp; English.  
XX This sequence represents an immunogenic peptide motif of beta-casein  
CC which is capable of mimicking a fragment of the GLUT2 protein found in  
CC insulin producing cells of the pancreas. There is a known correlation  
CC between exposure to cow's milk and the development of insulin-dependent  
CC diabetes which could possibly be linked to this molecular mimicry.  
CC Dietary or pharmaceutical products derived from milk substantially free  
CC of non-human beta casein or containing modified beta-casein without this  
CC motif could be used in diets for the prevention of insulin dependent  
CC diabetes particularly during early infancy.  
XX Sequence 4 AA;  
AAW31293 Length: 4 March 3, 2003 11:29 Type: P Check: 738 ..  
Initial Score = 3 Optimized Score = 3 Significance = -1.19  
Residue Identity = 75% Matches = 3 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0  
X X  
PGPIP  
||||  
GPIH  
X X  
17. US-09-095-639A-2 (1-5)  
p02662 Alpha-S1 casein precursor.  
TOIG of: p02662 check: 2471 from: 1 to: 214  
ID CAS1\_BOVIN STANDARD; PRT; 214 AA.  
AC P02662; Q28048;  
DT 21-JUL-1986 (Rel. 01, Created)  
DT 01-NOV-1990 (Rel. 16, Last sequence update)  
DT 01-MAR-2002 (Rel. 41, Last annotation update)  
DE Alpha-S1 casein precursor.  
GN CSNLS1.  
OS Bos taurus (Bovine).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;  
OC Bovidae; Bovinae; Bos.  
OX NCHI\_TaxID=9913;  
RN [1]  
RP SEQUENCE FROM N.A.  
RX MEDLINE=84221403; PubMed=6328443;

RA Stewart A.F., Willis I.M., Mackinlay A.G.;  
RT "Nucleotide sequences of bovine alpha S1- and kappa-casein cDNAs.";  
RL Nucleic Acids Res. 12:3895-3907(1984).  
RN [2]  
RP SEQUENCE FROM N.A.  
RA Nagao M., Maki M., Sasaki R., Chiba R.;  
RT "Isolation and sequence analysis of bovine alpha-S1-casein cDNA  
clone.";  
RL Agric. Biol. Chem. 48:1663-1667(1984).  
RN [3]  
RP SEQUENCE FROM N.A.  
RX MEDLINE=87049835; PubMed=3022833;  
RA Gorodetskii S.I., Zakhar'ev V.M., Kyarshulite D.R., Kapelinskaya T.V.,  
RA Skryabin K.G.;  
RT "cDNA of cattle alpha S1-casein: cloning and nucleotide sequence.";  
RL Biochimia 51:1641-1648(1986).  
RN [4]  
RP SEQUENCE FROM N.A.  
RX MEDLINE=92051301; PubMed=1658736;  
RA Kozzan D., Hobom G., Seyfert H.M.;  
RT "Genomic organization of the bovine alpha-S1 casein gene.";  
RL Nucleic Acids Res. 19:5591-5596(1991).  
RN [5]  
RP SEQUENCE OF 55-130 FROM N.A.  
RX MEDLINE=83182023; PubMed=6897774;  
RA Willis I.M., Stewart A.F., Caputo A., Thompson A.R., McKinlay A.G.;  
RT "Construction and identification by partial nucleotide sequence  
analysis of bovine casein and beta-lactoglobulin cDNA clones.";  
RL DNA 1:375-386(1982).  
RN [6]  
RP SEQUENCE OF 122-214 FROM N.A.  
RX MEDLINE=85178933; PubMed=3838718;  
RA Kiarshulite D.R., Zakhar'ev V.M., Gorodetskii S.I.;  
RT "Nucleotide sequence of the 3'-nontranslated region of the mRNA of  
alpha S1-casein in cows.";  
RL Dokl. Akad. Nauk SSSR 280:1433-1437(1985).  
RN [7]  
RP SEQUENCE OF 164-214 FROM N.A.  
RX MEDLINE=94154154; PubMed=1343827;  
RA Chen R., Wang B., Zhang Y., Liu W., Zhang J., Lao W.;  
RT "Cloning, mapping, and sequencing of 3' and its flanking region of  
bovine alpha-S1 casein gene.";  
RL Chin. J. Biotechnol. 8:235-245(1992).  
RN [8]  
RP SEQUENCE OF 16-214 (VARIANT B).  
RX MEDLINE=72063417; PubMed=4331376;  
RA Mercier J.-C., Grosclaude F., Ribadeau-Dumas B.;  
RT "Primary structure of bovine alpha-S1 casein. Complete sequence.";  
RL Eur. J. Biochem. 23:41-51(1971).  
RN [9]  
RP REVISIONS TO 74 AND 92-93 (VARIANTS A; B; C AND D).  
RX MEDLINE=74082545; PubMed=4797901;  
RA Mercier J.-C., Grosclaude F., Ribadeau-Dumas B.;  
RT "Primary structure of alpha casein and of bovine beta casein.  
Correction.";  
RL Eur. J. Biochem. 40:323-323(1973).  
RN [10]  
RP SEQUENCE (VARIANT D).  
RX MEDLINE=72214259; PubMed=5064450;  
RA Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;  
RT "Characterization of genetic variants of alpha-S1 and beta bovine  
caseins.";  
RL Eur. J. Biochem. 26:328-337(1972).  
RN [11]  
RP SEQUENCE OF 23-49 (VARIANT A).  
RX Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;  
RT "Localization in the N-terminal part of bovine casein alpha-S1 of a  
13 amino-acid deletion that differentiates variant A from variants B  
and C.";  
RL FEBS Lett. 11:109-112(1970).  
RN [12]  
RP SEQUENCE OF 205-214 (VARIANT C).  
RX Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.;

RT "On the localization in the C-terminal sequence of bovine casein  
alpha-S1 of a Glu/Gly substitution that differentiates the genetic  
variants B and C.";  
RL C. R. Acad. Sci., D, Sci. Nat. 268:3133-3136(1970).  
RN [13]  
RP REVISION (VARIANT C).  
RX Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.;  
RA C. R. Acad. Sci., D, Sci. Nat. 271:563-563(1970).  
RL -1- FUNCTION: IMPORTANT ROLE IN THE CAPACITY OF MILK TO TRANSPORT  
CALCIUM PHOSPHATE.  
CC -1- SUBCELLULAR LOCATION: Extracellular.  
CC -1- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.  
CC -1- MISCELLANEOUS: THE B VARIANT SEQUENCE IS SHOWN.  
CC -1- SIMILARITY: BELONGS TO THE ALPHA-CASEIN FAMILY.  
CC -1- DATABASE: NAME=worthington enzyme manual;  
WWW="http://www.worthington-biochem.com/manual/C/CASA.html".  
CC -1- DATABASE: NAME=proteinspotlight;  
NOTE=Issue 16 of November 2001;  
WWW="http://www.expasy.org/spotlight/articles/sptlt016.html".  
CC -----  
CC This SWISS-PROT entry is copyright. It is produced through a collaboration  
between the Swiss Institute of Bioinformatics and the EMBL outstation  
the European Bioinformatics Institute. There are no restrictions on its  
use by non-profit institutions as long as its content is in no way  
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entities requires a license agreement (See <http://www.isb-sib.ch/announce/>  
or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
CC -----  
DR EMBL; X00564; CAB57792.1; -;  
DR EMBL; M33123; AAA30428.1; -;  
DR EMBL; M38641; AAA30429.1; -;  
DR EMBL; X59856; CAA42516.1; -;  
DR EMBL; M10084; AAA30478.1; -;  
DR EMBL; M38658; AAA62707.1; -;  
DR EMBL; S72388; AAD14099.1; -;  
DR PIR; A03106; KABCOSB.  
DR PIR; A23071; A23071.  
DR PIR; S02202; S02202.  
DR PIR; S22575; S22575.  
DR InterPro; IPR001588; Casein.  
DR Pfam; PF00363; caseins; 1.  
DR PROSITE; PS00306; CASEIN\_ALPHA\_BETA; 1.  
KW Milk; Phosphorylation; Signal; Repeat.  
FT SIGNAL 1 15  
FT CHAIN 16 214 ALPHA-S1 CASEIN.  
FT MOD\_RES 61 61 PHOSPHORYLATION.  
FT MOD\_RES 63 63 PHOSPHORYLATION.  
FT MOD\_RES 68 68 PHOSPHORYLATION (IN VARIANT D).  
FT MOD\_RES 79 79 PHOSPHORYLATION.  
FT MOD\_RES 81 81 PHOSPHORYLATION.  
FT MOD\_RES 82 82 PHOSPHORYLATION.  
FT MOD\_RES 83 83 PHOSPHORYLATION.  
FT MOD\_RES 90 90 PHOSPHORYLATION.  
FT MOD\_RES 130 130 PHOSPHORYLATION.  
FT REPEAT 85 99  
FT REPEAT 125 140  
FT VARIANT 29 41 MISSING (IN VARIANT A).  
FT VARIANT 68 68 A -> T (IN VARIANT D).  
FT VARIANT 207 207 E -> G (IN VARIANT C).  
FT VARIANT 42 42 P -> L (IN REF. 3).  
FT CONFLICT 50 50 E -> Q (IN REF. 4 AND 11).  
FT CONFLICT 95 95 H -> Q (IN REF. 5).  
FT CONFLICT 143 143 H -> D (IN REF. 3).  
FT CONFLICT 203 203 S -> L (IN REF. 6).  
FT CONFLICT 211 212 MP -> IS (IN REF. 3).  
SQ SEQUENCE 214 AA; 24529 MW; F066B5C8AE55828B CRC64;  
P02662 Length: 214 February 28, 2003 14:33 Type: P Check: 2471 ..  
Initial Score = 3 Optimized Score = 4 Significance = -1.19  
Residue Identity = 60% Matches = 3 Mismatches = 2  
Caps = 0 Conservative Substitutions = 0

X X  
PGPIP  
| |  
YTDAPSFDPNPGISENSEKTTMP  
190 200 X 210

18. US-09-095-639A-2 (1-5)  
R37103 Bovine milk beta-casein enzymatic fragment.  
ID R37103 standard; peptide; 7 AA.  
AC R37103;  
DT 21-MAY-1995 (first entry)  
DE Bovine milk beta-casein enzymatic fragment.  
KW Beta-casein; enzymatic hydrolysate; cosmetics; skin disorders;  
wrinkles.  
OS Bos Taurus.  
PN J06166615-A.  
PD 14-JUN-1994.  
01-DEC-1992; 321624.  
01-DEC-1992; JP-321624.  
PA (POKK ) POLA CHEM IND INC.  
DR WPI; 94-230615/28.  
PT Cosmetics for treating skin disorders and wrinkles - containing  
enzymatic hydrolysate of human or bovine milk beta-casein  
Claim 2; Page 2; 7pp; Japanese.  
CC The invention relates to cosmetics containing human or bovine milk  
beta-casein enzymatic hydrolysate. The cosmetics are used for  
improving skin disorders and/or wrinkles. They are more effective  
than previously used polysaccharides, sugar alcohols, glycerol,  
glycols, etc.  
CC The present sequence is one component of the bovine milk beta-casein  
enzymatic hydrolysate.  
SQ Sequence 7 AA;  
SQ 1 A; 1 R; 0 N; 0 D; 0 B; 0 C; 1 Q; 0 E; 0 Z; 0 G; 0 H;  
SQ 0 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 1 Y; 1 V;  
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:04-PST using FindSeq  
Initial Score = 2 Optimized Score = -2.38  
Residue Identity = 40% Matches = 2 Mismatches = 3  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIP  
| |  
AVPYFQR  
X X









[illegible]

6. US-09-095-639A-3 (1-12)  
Bovine beta casein variant A2 immunogenic peptide.  
W31290

ID W31290 standard; peptide; 12 AA.  
AC W31290;  
DT 05-MAR-1998 (first entry)  
DE Bovine beta casein variant A2 immunogenic peptide.  
KW A2 variant beta-casein; immunogenic; molecular mimicry; cow;  
OS milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
OS Bos indicus.  
PN WO9724371-A1.  
PD 10-JUL-1997.  
PF 27-DEC-1996; E05846.  
PR 27-DEC-1995; IT-RM0850.  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
PI Pozzilli P;  
PI WPI; 97-363622/33.  
DR Beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
CC Claim 5: Page 4; 34pp; English.  
CC This sequence represents an immunogenic peptide from the A2 variant of  
CC beta-casein found in both Bos taurus and Bos indicus. The peptide  
CC contains a motif (see W31288) corresponding to amino acids 63-68 of the  
CC A2 beta casein protein and is found to be capable of mimicking a fragment  
CC of the GLUT2 protein found in insulin producing cells of the pancreas.  
CC There is a known correlation between exposure to cow's milk and the  
CC development of insulin-dependent diabetes which could possibly be linked  
CC to this molecular mimicry. Dietary or pharmaceutical products derived  
CC from milk substantially free of non-human beta casein or containing  
CC modified beta-casein without this motif could be used in diets for the  
CC prevention of insulin dependent diabetes particularly during early  
CC infancy.

Sequence 12 AA;  
SQ 0 A; 0 R; 1 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 0 H;  
SQ 1 I; 1 L; 0 K; 0 M; 1 F; 4 P; 1 S; 0 T; 0 W; 1 Y; 1 V;  
SQ Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq  
CC Initial Score = 11 Optimized Score = 11 Significance = 1.03  
Residue Identity = 91% Matches = 11 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

7. US-09-095-639A-3 (1-12)  
Bovine beta casein variant A2 immunogenic peptide.  
aaw31290

TOIG of: aaw31290 check: 6063 from: 1 to: 12  
ID AAW31290 standard; peptide; 12 AA.  
XX  
AC AAW31290;  
XX  
XX 05-MAR-1998 (first entry)  
XX Bovine beta casein variant A2 immunogenic peptide.  
DE A2 variant beta-casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
XX Bos taurus.  
OS Bos indicus.  
OS  
PN WO9724371-A1.  
XX  
PD 10-JUL-1997.

Initial Score = 12  
Residue Identity = 100%  
Gaps = 0  
Optimized Score = 12  
Matches = 12  
Mismatches = 0  
Significance = 1.29

8. US-09-095-639A-3 (1-12)  
Bovine beta casein variant A1 immunogenic peptide.  
aar95609

TOIG of: aar95609 check: 209 from: 1 to: 209  
ID AAR95609 standard; protein; 209 AA.  
AC AAR95609;  
XX  
XX 26-NOV-1996 (first entry)  
XX Bovine beta casein A1 variant.  
DE Milk; beta casein; diabetogenic; diabetes; cow; milk products;  
KW butter; cheese; cream.  
XX Bos taurus.  
XX  
XX Location/Qualifiers  
XX 63..68  
XX /label= Diabetogenic hexapeptide.  
XX  
XX WO9614577-A1.  
XX  
XX 17-MAY-1996.  
XX  
XX 03-NOV-1995; 95WO-NZ00114.  
XX  
XX 04-NOV-1994; 94NZ-0264862.  
XX  
XX (NACH-) NAT CHILD HEALTH RES FOUND.  
XX (NZDA-) NEW ZEALAND DAIRY BOARD.  
XX  
XX Elliott RB, Hill JP;  
XX WPI; 1996-251885/25.  
XX  
XX Selecting non-diabetogenic milk and milk prods. - by testing milk or  
XX cows for the presence of non-diabetogenic variants of beta-casein  
XX  
XX Disclosure; Figure 2; 28pp; English.

A method for selecting milk for feeding to diabetes susceptible  
CC individuals comprises testing milk from identified cows for the  
CC presence of variants of beta casein and selecting those cows whose  
CC milk contains non-diabetogenic variants and milking these cows  
CC separately. The milk and milk products obtained can reduce the risk  
CC of susceptible individuals contracting Type-1 diabetes.

Sequence 209 AA;  
AAR95609 Length: 209 March 3, 2003 11:28 Type: P Check: 2014  
Initial Score = 12 Optimized Score = 12 Significance = 1.29  
Residue Identity = 100% Matches = 12 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0

9. US-09-095-639A-3 (1-12)  
Bovine beta casein A1 variant.  
aar95609

TOIG of: aar95609 check: 2014 from: 1 to: 209  
ID AAR95609 standard; protein; 209 AA.  
AC AAR95609;  
XX  
XX 26-NOV-1996 (first entry)  
XX Bovine beta casein A1 variant.  
DE Milk; beta casein; diabetogenic; diabetes; cow; milk products;  
KW butter; cheese; cream.  
XX Bos taurus.  
XX  
XX Location/Qualifiers  
XX 63..68  
XX /label= Diabetogenic hexapeptide.  
XX  
XX WO9614577-A1.  
XX  
XX 17-MAY-1996.  
XX  
XX 03-NOV-1995; 95WO-NZ00114.  
XX  
XX 04-NOV-1994; 94NZ-0264862.  
XX  
XX (NACH-) NAT CHILD HEALTH RES FOUND.  
XX (NZDA-) NEW ZEALAND DAIRY BOARD.  
XX  
XX Elliott RB, Hill JP;  
XX WPI; 1996-251885/25.  
XX  
XX Selecting non-diabetogenic milk and milk prods. - by testing milk or  
XX cows for the presence of non-diabetogenic variants of beta-casein  
XX  
XX Disclosure; Figure 2; 28pp; English.

XX 27-DEC-1996; 96WO-EP05846.  
 XX  
 XX 27-DEC-1995; 95IT-0RM0850.  
 XX  
 XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
 XX (MIDI-) MIDIA LTD.  
 XX  
 XX Pozzilli P;  
 XX  
 XX WPI; 1997-363622/33.  
 XX  
 XX Beta-casein or fragments not showing mimicry with GLUT2 - used in  
 XX food or pharmaceutical products for prevention of insulin dependent  
 XX diabetes, particularly in early infancy  
 XX  
 XX Claim 5; Page 4; 34pp; English.  
 XX  
 XX This sequence represents an immunogenic peptide from the A2 variant of  
 XX beta-casein found in both Bos taurus and Bos indicus. The peptide  
 XX contains a motif (see AAW31288), corresponding to amino acids 63-68 of  
 XX the A2 beta casein protein and is found to be capable of mimicking a  
 XX fragment of the GLUT2 protein found in insulin producing cells of the  
 XX pancreas. There is a known correlation between exposure to cow's milk and  
 XX the development of insulin-dependent diabetes which could possibly be  
 XX linked to this molecular mimicry. Dietary or pharmaceutical products  
 XX derived from milk substantially free of non-human beta casein or  
 XX containing modified beta-casein without this motif could be used in diets  
 XX for the prevention of insulin dependent diabetes particularly during  
 XX early infancy.  
 XX  
 XX SQ Sequence 12 AA;  
 XX  
 XX AAW31290 Length: 12 March 3, 2003 11:29 Type: P Check: 6063  
 XX  
 XX Initial Score = 11 Optimized Score = 11 Significance = 1.03  
 XX Residue Identity = 91% Matches = 11 Mismatches = 1  
 XX Gaps = 0 Conservative Substitutions = 0  
 XX  
 XX X 10 X  
 XX SLVYPPGPPTHN  
 XX |||||  
 XX SLVYPPGPPIPN  
 XX X 10 X

8. US-09-095-639a-3 (1-12)  
 P02666 Beta casein precursor.  
 ORIG of: p02666 check: 8112 from: 1 to: 224

ID CASE\_BOVIN STANDARD; PRT; 224 AA.  
 AC P02666;  
 DT 21-JUL-1986 (Rel. 01, Created)  
 DT 01-MAR-1989 (Rel. 10, Last sequence update)  
 DT 01-MAR-2002 (Rel. 41, Last annotation update)  
 DE Beta casein precursor.  
 GN CSN2.  
 OS Bos taurus (Bovine).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;  
 OC Bovidae; Bovinae; Bos.  
 OC NCBI\_TaxID=9913;  
 RN (1)  
 RN SEQUENCE FROM N.A.  
 RA Baev A.A., Smirnov I.K., Gorodetsky S.I.;  
 RT "Primary structure of bovine beta-casein cDNA."  
 RL Mol. Biol. (Mosk) 21:214-222(1987).  
 RN (2)  
 RN SEQUENCE FROM N.A.  
 RA MEDLINE=8818989; PubMed=2833669;  
 RX Stewart A.F., Bonsing J., Beattie C.W., Shah F., Willis I.M.,  
 RA Mackinlay A.G.;

RT "Complete nucleotide sequences of bovine alpha S2- and beta-casein  
 RL cDNAs: comparisons with related sequences in other species.";  
 RL Mol. Biol. Evol. 4:231-241(1987).  
 RN (3)  
 RN SEQUENCE FROM N.A.  
 RP MEDLINE=90147279; PubMed=3271384;  
 RX Bonsing J., Ring J.M., Stewart A.F., Mackinlay A.G.;  
 RA "Complete nucleotide sequence of the bovine beta-casein gene.";  
 RT Aust. J. Biol. Sci. 41:527-537(1988).  
 RN (4)  
 RN SEQUENCE FROM N.A.  
 RP MEDLINE=87128158; PubMed=3814153;  
 RX Jimenez-Flores R., Kang Y.C., Richardson T.;  
 RA "Cloning and sequence analysis of bovine beta-casein cDNA.";  
 RT Biochem. Biophys. Res. Commun. 142:617-621(1987).  
 RN (5)  
 RN SEQUENCE FROM N.A. (VARIANT A3).  
 RP TISSUE-Mammary gland;  
 RC MEDLINE=94088382; PubMed=8248100;  
 RA Simons G., van den Heuvel W., Reynen T., Frijters A., Rutten G.,  
 RA Slangen C.J., Groenen M., de Vos W.M., Siezen R.J.;  
 RT "Overproduction of bovine beta-casein in Escherichia coli and  
 RL engineering of its main chymosin cleavage site.";  
 RL Protein Eng. 6:763-770(1993).  
 RN (6)  
 RN SEQUENCE OF 16-224 (VARIANT A2).  
 RP MEDLINE=88152252; PubMed=3278933;  
 RX Carles C., Huet J.-C., Ribadeau-Dumas B.;  
 RA "A new strategy for primary structure determination of proteins:  
 RT application to bovine beta-casein.";  
 RL FEBS Lett. 229:265-272(1988).  
 RN (7)  
 RN SEQUENCE OF 16-224 (VARIANT A2).  
 RP MEDLINE=72232212; PubMed=4557764;  
 RX Ribadeau-Dumas B., Brignon G., Grosclaude F., Mercier J.-C.;  
 RA "Primary structure of bovine beta casein. Complete sequence.";  
 RL Eur. J. Biochem. 25:505-514(1972).  
 RN (8)  
 RN VARIANTS A1; B AND C.  
 RP MEDLINE=72214259; PubMed=5064450;  
 RX Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;  
 RA "Characterization of genetic variants of alpha-SI and beta bovine  
 RL caseins.";  
 RL Eur. J. Biochem. 26:328-337(1972).  
 RN (9)  
 RN SEQUENCE OF 118-124 (VARIANT A3).  
 RP MEDLINE=71252171; PubMed=4997616;  
 RX Ribadeau-Dumas B., Grosclaude F., Mercier J.-C.;  
 RA "Localization in the peptide chain of bovine beta casein of the  
 RT His-Gln substitution differentiating the A2 and A3 genetic  
 RL variants.";  
 RL C. R. Acad. Sci., D, Sci. Nat. 270:2369-2372(1970).  
 RN (10)  
 RN SEQUENCE OF 48-63 (VARIANT E).  
 RP MEDLINE=75005247; PubMed=4411121;  
 RX Grosclaude F., Mahe M.-F., Voglino G.-F.;  
 RA "The beta E variant and the phosphorylation code of bovine caseins.";  
 RL FEBS Lett. 45:3-5(1974).  
 RN (11)  
 RN SEQUENCE OF 68-105 FROM N.A.  
 RP MEDLINE=85155504; PubMed=6397405;  
 RX Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,  
 RA Sulimova G.E., Judinkova E.S., Gorodetsky S.I.;  
 RT "Identification of bacterial clones encoding bovine caseins by direct  
 RL immunological screening of the cDNA library.";  
 RL Gene 32:381-388(1984).  
 RN (12)  
 RN SEQUENCE OF 68-95 FROM N.A.  
 RP MEDLINE=86014005; PubMed=3900695;  
 RX Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,  
 RA Silimova G.E.;  
 RT "Identification of bacterial clones coding for bovine caseins by  
 RL direct immunologic screening of the cDNA library.";

RL Mol. Biol. (Mosk) 19:955-963(1985).  
RN [13]  
RP SEQUENCE OF 18-57 FROM N.A., AND SEQUENCE OF 16-224 (VARIANT H).  
RA MEDLINE=20154951; PubMed=10690361;  
RX Han S.K., Shin Y.C., Byun H.D.;  
RT "Biochemical, molecular and physiological characterization of a new  
RT beta-casein variant detected in Korean cattle.";  
RL Anim. Genet. 31:49-51(2000).  
RN [14]  
RP SEQUENCE OF 125-195 (VARIANTS A1 AND G).  
RA Dong C., Ng-Kwai-Hang K.F.;  
RT "Characterization of a non-electrophoretic genetic variant of beta-  
RT casein by peptide mapping and mass spectrometric analysis.";  
RL Int. Dairy J. 8:967-972(1998).  
RN [15]  
RP SEQUENCE OF 160-171 (VARIANT F).  
RA MEDLINE=96118672; PubMed=7496485;  
RX Visser S., Slangen C.J., Lagerwerf F.M., Van Dongen W.D.,  
RA Haverkamp J.;  
RT "Identification of a new genetic variant of bovine beta-casein using  
RT reversed-phase high-performance liquid chromatography and mass  
RT spectrometric analysis.";  
RL J. Chromatogr. A 711:141-150(1995).  
RN [16]  
RP SEQUENCE OF 170-184 FROM N.A.  
RX MEDLINE=83182023; PubMed=6897774;  
RA Willis I.M., Stewart A.F., Caputo A., Thompson A.R., McKinlay A.G.;  
RT "Construction and identification by partial nucleotide sequence  
RT analysis of bovine casein and beta-lactoglobulin cDNA clones";  
RL DNA 1:375-386(1982).  
RN [17]  
RP CARBOHYDRATE-LINKAGE SITES  
RX MEDLINE=85000478; PubMed=6148101;  
RA Yan S.B., Wold F.;  
RT "Neoglycoproteins: In vitro introduction of glycosyl units at  
RT glutamines in beta-casein using transglutaminase.";  
RL Biochemistry 23:3759-3765(1984).  
\*CC -!- FUNCTION: IMPORTANT ROLE IN DETERMINATION OF THE SURFACE  
CC PROPERTIES OF THE CASEIN MICELLES.  
CC -!- SUBCELLULAR LOCATION: Extracellular.  
CC -!- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.  
CC -!- POLYMORPHISM: LEU-152 IS PRESENT IN THE VARIANTS F AND G; GLN-190  
CC AND GLU-210 ARE PRESENT IN THE VARIANT H. THE SEQUENCE SHOWN IS  
CC THE A2 VARIANT.  
CC -!- SIMILARITY: BELONGS TO THE BETA-CASEIN FAMILY.  
CC -!- DATABASE: NAME-Protein Spotlight;  
CC NOTE-Issue 16 of November 2001;  
CC WWW="http://www.expasy.org/spotlight/articles/sptlt016.html".  
-----  
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-----  
EMBL; M16645; AAA30480.1; -  
EMBL; M15132; AAA30430.1; -  
EMBL; K01087; AAA30481.1; -  
EMBL; X06359; CAA29658.1; -  
EMBL; M55158; AAA30431.1; -  
EMBL; S67277; AAB29137.1; -  
EMBL; AF104929; AAD09813.1; -  
EMBL; AF104928; AAD09813.1; JOINED.  
DR EMBL; M64756; AAB59254.1; -  
DR PIR; A03110; KBB0A2.  
DR PIR; A25846; A25846.  
DR PIR; B29087; B29087.  
DR PIR; S01860; S01860.  
DR PIR; S02429; S02429.  
DR CarBank; CCSD:9067; -  
DR InterPro; IPR001588; Casein.

DR Pfam; PF00363; caseins; 1.  
DR PROSITE; PS00306; CASEIN\_ALPHA\_BETA; 1.  
KW Milk; Phosphorylation; Glycoprotein; Signal; Polymorphism.  
FT SIGNAL 1 15  
FT CHAIN 16 224 BETA CASEIN.  
FT MOD\_RES 30 30 PHOSPHORYLATION.  
FT MOD\_RES 32 32 PHOSPHORYLATION.  
FT MOD\_RES 33 33 PHOSPHORYLATION.  
FT MOD\_RES 34 34 PHOSPHORYLATION.  
FT MOD\_RES 50 50 PHOSPHORYLATION (EXCEPT IN VARIANT C).  
FT CARBOHYD 70 70 O-LINKED (GALNAC. . .) (PARTIAL).  
FT CARBOHYD 72 72 O-LINKED (GALNAC. . .).  
FT CARBOHYD 95 95 O-LINKED (GALNAC. . .).  
FT CARBOHYD 183 183 O-LINKED (GALNAC. . .).  
FT VARIANT 40 40 R -> C (IN VARIANT H).  
FT VARIANT 51 51 E -> K (IN VARIANT E).  
FT VARIANT 52 52 E -> K (IN VARIANT C).  
FT VARIANT 82 82 P -> H (IN VARIANTS A1, B, C, F AND G).  
FT VARIANT 103 103 L -> I (IN VARIANT H).  
FT VARIANT 121 121 H -> Q (IN VARIANT A3).  
FT VARIANT 132 132 E -> Q (IN VARIANTS A1 AND G).  
FT VARIANT 137 137 S -> R (IN VARIANT B).  
FT VARIANT 152 153 LP -> PL (IN VARIANTS A1 AND H).  
FT VARIANT 153 153 P -> L (IN VARIANT G).  
FT VARIANT 167 167 P -> L (IN VARIANT F).  
FT VARIANT 190 190 Q -> E (IN VARIANTS A1 AND G).  
FT CONFLICT 108 108 M -> L (IN REF. 4 AND 7).  
FT CONFLICT 210 210 E -> Q (IN REF. 4 AND 7).  
FT CONFLICT 215 224 PVRGPFPIIV -> DPSLLL (IN REF. 1).  
SQ SEQUENCE 224 AA; 25107 MW; FOBBDD8148A238AE CRC64;  
P02666 Length: 224 February 28, 2003 14:33 Type: P Check: 8112 ..  
Initial Score = 11 Optimized Score = 11 Significance = 1.03  
Residue Identity = 91% Matches = 11 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0  
X 10 X  
SLVYPPFGPIHN  
|||||||  
DKTHPFAQTQSLVYPPFGPIHNSLPONIPPLT  
70 X 80 X 90  
9. US-09-095-639A-3 (1-12)  
p02662 Alpha-S1 casein precursor.  
TOIG of: p02662 check: 2471 from: 1 to: 214

ID CAS1\_BOVIN STANDARD; PRT; 214 AA.  
AC P02662; Q28048;  
DT 21-JUL-1986 (Rel. 01, Created)  
DT 01-NOV-1990 (Rel. 16, Last sequence update)  
DT 01-MAR-2002 (Rel. 41, Last annotation update)  
DE Alpha-S1 casein precursor.  
GN CSNIS1.  
OS Bos taurus (Bovine).  
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;  
OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;  
OC Bovidae; Bovinae; Bos.  
OX NCBI\_TaxID=9913;  
RN [1]  
RP SEQUENCE FROM N.A.  
RX MEDLINE=84221403; PubMed=6328443;  
RA Stewart A.F., Willis I.M., Mackinlay A.G.;  
RT "Nucleotide sequences of bovine alpha S1- and kappa-casein cDNAs.";  
RL Nucleic Acids Res. 12:3895-3907(1984).  
RN [2]  
RP SEQUENCE FROM N.A.  
RA Nagao M., Maki M., Sasaki R., Chiba R.;  
RT "Isolation and sequence analysis of bovine alpha-S1-casein cDNA  
RT clone.";  
RL Agric. Biol. Chem. 48:1663-1667(1984).



W31287 standard; peptide; 5 AA.

W31287; (first entry)

Bovine beta casein variant A1 immunogenic peptide motif.

Al variant beta casein; immunogenic; molecular mimicry; cow;

milk product; insulin-dependent diabetes; GLUT2; diet.

Bos taurus.

WO9724371-AL.

10-JUL-1997.

27-DEC-1996; E05846.

27-DEC-1995; IT-RM0850.

(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

(MIDI-) MIDIA LTD.

Pozzilli P;

WPI; 97-363622/33.

Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

Claim 5; Page 3; 34pp; English.

This sequence represents an immunogenic peptide motif from the A1 variant of beta-casein which is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

Sequence 5 AA;

AAW31287 Length: 5 March 3, 2003 11:29 Type: P Check: 1114 ..

Initial Score = 5 Optimized Score = -0.52

Residue Identity = 100% Matches = 5 Mismatches = 0

Gaps = 0 Conservative Substitutions = 0

X 10

SLVYPPFGPIHN

|||||

PGPIH

X X

12. US-09-095-639A-3 (1-12)

W31293 Bovine beta casein immunogenic peptide motif 1.

W31293 standard; peptide; 4 AA.

W31293;

05-MAR-1998 (first entry)

Bovine beta casein immunogenic peptide motif 1.

Beta casein; immunogenic; molecular mimicry; cow;

milk product; insulin-dependent diabetes; GLUT2; diet.

Bos taurus.

WO9724371-AL.

10-JUL-1997.

27-DEC-1996; E05846.

27-DEC-1995; IT-RM0850.

(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

(MIDI-) MIDIA LTD.

Pozzilli P;

WPI; 97-363622/33.

Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

Claim 10; Page 6; 34pp; English.

This sequence represents an immunogenic peptide motif of beta-casein which is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

Sequence 4 AA;

SQ 0 A; 0 R; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 1 H;

SQ 1 I; 0 L; 0 K; 0 M; 0 F; 1 P; 0 S; 0 T; 0 W; 0 Y; 0 V;

Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 4 Optimized Score = -0.78

W31287 standard; peptide; 5 AA.

W31287; (first entry)

Bovine beta casein variant A1 immunogenic peptide motif.

Al variant beta casein; immunogenic; molecular mimicry; cow;

milk product; insulin-dependent diabetes; GLUT2; diet.

Bos taurus.

WO9724371-AL.

10-JUL-1997.

27-DEC-1996; E05846.

27-DEC-1995; IT-RM0850.

(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

(MIDI-) MIDIA LTD.

Pozzilli P;

WPI; 97-363622/33.

Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

Claim 5; Page 3; 34pp; English.

This sequence represents an immunogenic peptide motif from the A1 variant of beta-casein which is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

Sequence 5 AA;

Initial Score = 5 Optimized Score = -0.52

Residue Identity = 100% Matches = 5 Mismatches = 0

Gaps = 0 Conservative Substitutions = 0

X 10

SLVYPPFGPIHN

|||||

PGPIH

X X

11. US-09-095-639A-3 (1-12)

aaw31287 Bovine beta casein variant A1 immunogenic peptide

W31287

W31287 standard; peptide; 5 AA.

W31287;

05-MAR-1998 (first entry)

Bovine beta casein variant A1 immunogenic peptide motif.

Al variant beta casein; immunogenic; molecular mimicry; cow;

milk product; insulin-dependent diabetes; GLUT2; diet.

Bos taurus.

WO9724371-AL.

10-JUL-1997.

27-DEC-1996; 96WO-EP05846.

27-DEC-1995; 95IT-ORM0850.

(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

(MIDI-) MIDIA LTD.





Mon Mar 3 11:50:09 2003

Initial Score = 4 Optimized Score = 4 Significance = -0.78  
Residue Identity = 28% Matches = 2 Mismatches = 4  
Gaps = 0 Conservative Substitutions = 1

27-DEC-1996; 96WO-EP05846.  
27-DEC-1995; 95TP-OR0850.  
(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
(MIDI-) MIDIA LTD.  
Pozzilli P;  
WPI; 1997-363622/33.

Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

Claim 5; Page 4; 34pp; English.

This sequence represents an immunogenic peptide motif from the A2 variant beta-casein found in both Bos taurus and Bos indicus (amino acid position 63-68). This motif is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

Sequence 5 AA;

AAW31288 Length: 5 March 3, 2003 11:28 Type: P Check: 1154

Initial Score = 4 Optimized Score = 4 Significance = -0.78  
Residue Identity = 80% Matches = 4 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X 10

SLVYFPFGPIHN  
||||  
FGPIP  
X X

16. US-09-095-639A-3 (1-12)  
R37103 Bovine milk beta-casein enzymatic fragment.

R37103 standard; peptide; 7 AA.

21-MAY-1995 (first entry)  
Bovine milk beta-casein enzymatic fragment.  
Beta-casein; enzymatic hydrolysate; cosmetics; skin disorders; wrinkles.

OS Bos Taurus.  
PN J06166615-A.  
PD 14-JUN-1994.  
PF 01-DEC-1992; 321624.  
PR 01-DEC-1992; JP-321624.  
PA (POKK) POLA CHEM IND INC.  
DR WPI; 94-230615/28.  
PT Cosmetics for treating skin disorders and wrinkles - containing enzymatic hydrolysate of human or bovine milk beta-casein

PS Claim 2; Page 2; 7pp; Japanese.  
CC The invention relates to cosmetics containing human or bovine milk beta-casein enzymatic hydrolysate. The cosmetics are used for improving skin disorders and/or wrinkles. They are more effective than previously used polysaccharides, sugar alcohols, glycerol, glycols, etc.  
CC The present sequence is one component of the bovine milk beta-casein enzymatic hydrolysate.

SQ Sequence 7 AA;  
SQ 1 A; 1 R; 0 N; 0 D; 0 B; 0 C; 1 Q; 0 E; 0 Z; 0 G; 0 H;  
SQ 0 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 1 Y; 1 V;  
Retrieved by bobyen on Thu 27 Feb 103 16:22:04-PST using FindSeq

17. US-09-095-639A-3 (1-12)  
W31294 Bovine beta casein immunogenic peptide motif 2.

W31294 standard; peptide; 4 AA.

ID W31294; 1998 (first entry)  
AC 05-MAR-1998 (first entry)  
DE Bovine beta casein immunogenic peptide motif 2.  
KW Beta-casein; immunogenic; molecular mimicry; cow;  
OS Bos taurus.  
PN W09724371-A1.  
PD 10-JUL-1997; E05846.  
PF 27-DEC-1996; IT-NM0850.  
PR (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
PI Pozzilli P;  
DR WPI; 97-363622/33.

PT Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy  
PT Claim 10; Page 6; 34pp; English.  
CC This sequence represents an immunogenic peptide motif found in bovine beta casein. This motif is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

Sequence 4 AA;

SQ 0 A; 0 R; 0 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 0 H;  
SQ 1 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
Retrieved by bobyen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 3 Optimized Score = 3 Significance = -1.03  
Residue Identity = 75% Matches = 3 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

10  
SLVYFPFGPIHN  
||||  
FGPIP  
X X

18. US-09-095-639A-3 (1-12)  
aaw31294 Bovine beta casein immunogenic peptide motif 2.

TOIG of: aaw31294 check: 770 from: 1 to: 4

ID AAW31294 standard; peptide; 4 AA.

AC AAW31294;  
XX 05-MAR-1998 (first entry)

DE Bovine beta casein immunogenic peptide motif 2.  
KW Beta-casein; immunogenic; molecular mimicry; cow;

KW milk product; insulin-dependent diabetes; GLUT2; diet.

XX OS Bos taurus.

XX PN W09724371-A1.

XX PD 10-JUL-1997.

XX PF 27-DEC-1996; 96WO-EP05846.

XX PR 27-DEC-1995; 95IT-ORM0850.

XX PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

XX PA (MIDI-) MIDIA LTD.

XX PI Pozzilli P;

XX DR WPI; 1997-363622/33.

XX Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

XX Claim 10; Page 6; 34pp; English.

XX This sequence represents an immunogenic peptide motif found in bovine beta casein. This motif is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

XX Sequence 4 AA;

. AAW31294 Length: 4 March 3, 2003 11:28 Type: P Check: 770 ..

Initial Score	=	3	Optimized Score	=	-1.03
Residue Identity	=	75%	Matches	=	3
Gaps	=	0	Mismatches	=	1
			Conservative Substitutions	=	0

10  
SLVYPPFGPIHN  
|||  
GPIP  
X X





SQ 1 I; 1 L; 0 K; 0 M; 1 F; 4 P; 1 S; 0 T; 0 W; 1 Y; 1 V;  
 CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 12 Optimized Score = 12 Significance = 1.33  
 Residue Identity = 100% Matches = 12 Mismatches = 0  
 Gaps = 0 Conservative Substitutions = 0

X 10 X  
 SLVYPPGPIP  
 |||||  
 SLVYPPGPIP  
 X 10 X

2. US-09-095-639A-4 (1-12)  
 aaw31290 Bovine beta casein variant A2 immunogenic peptide.

TOIG of: aaw31290 check: 6063 from: 1 to: 12

AAW31290 standard; peptide; 12 AA.

AAW31290;

05-MAR-1998 (first entry)

Bovine beta casein variant A2 immunogenic peptide.

A2 variant beta-casein; immunogenic; molecular mimicry; cow;  
 milk product; insulin-dependent diabetes; GLUT2; diet.

Bos taurus.  
 Bos indicus.

W09724371-A1.

10-JUL-1997.

27-DEC-1996; 96WO-EP05846.

27-DEC-1995; 95IT-ORM0850.

(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
 (MIDI-) MIDIA LTD.

Pozzilli P;

WPI; 1997-363622/33.

Beta-casein or fragments not showing mimicry with GLUT2 - used in  
 food or pharmaceutical products for prevention of insulin dependent  
 diabetes, particularly in early infancy

Claim 5; Page 4; 34pp; English.

This sequence represents an immunogenic peptide from the A2 variant of  
 beta-casein found in both Bos taurus and Bos indicus. The peptide  
 contains a motif (see AAW31288) corresponding to amino acids 63-68 of  
 the A2 beta casein protein and is found to be capable of mimicking a  
 fragment of the GLUT2 protein found in insulin producing cells of the  
 pancreas. There is a known correlation between exposure to cow's milk and  
 the development of insulin-dependent diabetes which could possibly be  
 linked to this molecular mimicry. Dietary or pharmaceutical products  
 derived from milk substantially free of non-human beta casein or  
 containing modified beta-casein without this motif could be used in diets  
 for the prevention of insulin dependent diabetes particularly during  
 early infancy.

Sequence 12 AA;

AAW31290 Length: 12 March 3, 2003 11:29 Type: P Check: 6063

Initial Score = 12 Optimized Score = 12 Significance = 1.33  
 Residue Identity = 100% Matches = 12 Mismatches = 0

Gaps

X 10 X  
 SLVYPPGPIP  
 |||||  
 SLVYPPGPIP  
 X 10 X

3. US-09-095-639A-4 (1-12)  
 p02666 Beta casein precursor.

TOIG of: p02666 check: 8112 from: 1 to: 224

ID CASB BOVIN STANDARD; PRT; 224 AA.

AC P02666;

DT 21-JUL-1986 (Rel. 01, Created)

DT 01-MAR-1989 (Rel. 10, Last sequence update)

DT 01-MAR-2002 (Rel. 41, Last annotation update)

DE Beta casein precursor.

GN CSN2.

OS Bos taurus (Bovine).

OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;

OC Bovidae; Bovinae; Bos.

OX NCBI\_TaxID=9913;

RN [1]

RP SEQUENCE FROM N.A.

RA Baev A.A., Smirnov I.K., Gorodetsky S.I.;

RT "Primary structure of bovine beta-casein cDNA.";

RL Mol. Biol. (Mosk) 21:214-222(1987).

RN [2]

RP SEQUENCE FROM N.A.

RX MEDLINE=88188989; PubMed=2833669;

RA Stewart A.F., Bonsing J., Beattie C.W., Shah F., Willis I.M.,

RA Mackinlay A.G.;

RT "Complete nucleotide sequences of bovine alpha S2- and beta-casein  
 cDNAs: comparisons with related sequences in other species.";

RL Mol. Biol. Evol. 4:231-241(1987).

RN [3]

RP SEQUENCE FROM N.A.

RX MEDLINE=90147279; PubMed=3271384;

RA Bonsing J., Ring J.M., Stewart A.F., Mackinlay A.G.;

RT "Complete nucleotide sequence of the bovine beta-casein gene.";

RL Aust. J. Biol. Sci. 41:527-537(1988).

RN [4]

RP SEQUENCE FROM N.A.

RX MEDLINE=87128158; PubMed=3814153;

RA Jimenez-Flores R., Kang Y.C., Richardson T.;

RT "Cloning and sequence analysis of bovine beta-casein cDNA.";

RL Biochem. Biophys. Res. Commun. 142:617-621(1987).

RN [5]

RP SEQUENCE FROM N.A. (VARIANT A3).

RC TISSUE=Mammary gland;

RX MEDLINE=94068382; PubMed=8248100;

RA Simons G., van den Heuvel W., Reynen T., Frijters A., Rutten G.,

RA Slangen C.J., Groenen M., de Vos W.M., Siezen R.J.;

RT "Overproduction of bovine beta-casein in Escherichia coli and

RT engineering of its main chymosin cleavage site.";

RL Protein Eng. 6:763-770(1993).

RN [6]

RP SEQUENCE OF 16-224 (VARIANT A2).

RX MEDLINE=88152252; PubMed=3278933;

RA Carles C., Huet J.-C., Ribadeau-Dumas B.;

RT "A new strategy for primary structure determination of proteins:

RT application to bovine beta-casein.";

RL FEBS Lett. 229:265-272(1988).

RN [7]

RP SEQUENCE OF 16-224 (VARIANT A2).

RX MEDLINE=7223212; PubMed=4557764;

RA Ribadeau-Dumas B., Brignon G., Grosclaude F., Mercier J.-C.;

RT "Primary structure of bovine beta casein. Complete sequence.";

RL Eur. J. Biochem. 25:505-514(1972).

RA VARIANTS A1; B AND C.  
RX MEDLINE=72214259; PubMed=5064450;  
RA Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;  
RT "Characterization of genetic variants of alpha-S1 and beta bovine  
RT caseins.";  
RL Eur. J. Biochem. 26:328-337(1972).  
[9]  
RN SEQUENCE OF 118-124 (VARIANT A3).  
RX MEDLINE=7252171; PubMed=4997616;  
RA Ribadeau-Dumas B., Grosclaude F., Mercier J.-C.;  
RT "Localization in the peptide chain of bovine beta casein of the  
RT His-Gln substitution differentiating the A2 and A3 genetic  
RT variants.";  
RL C. R. Acad. Sci., D, Sci. Nat. 270:2369-2372(1970).  
[10]  
RN SEQUENCE OF 48-63 (VARIANT E).  
RX MEDLINE=75005247; PubMed=4411121;  
RA Grosclaude F., Mahe M.-F., Voglino G.-F.;  
RT "The beta E variant and the phosphorylation code of bovine caseins.";  
RL FEBS Lett. 45:3-5(1974).  
[11]  
RN SEQUENCE OF 68-105 FROM N.A.  
RX MEDLINE=85155504; PubMed=6397405;  
RA Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,  
RA Sulimova G.E., Judinkova E.S., Gorodetsky S.I.;  
RT "Identification of bacterial clones encoding bovine caseins by direct  
RT immunological screening of the cDNA library.";  
RL Gene 32:381-388(1984).  
[12]  
RN SEQUENCE OF 68-95 FROM N.A.  
RX MEDLINE=86014005; PubMed=3900695;  
RA Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,  
RA Sulimova G.E.;  
RT "Identification of bacterial clones coding for bovine caseins by  
RT direct immunologic screening of the cDNA library.";  
RL Mol. Biol. (Mosk) 19:955-963(1985).  
[13]  
RN SEQUENCE OF 18-57 FROM N.A., AND SEQUENCE OF 16-224 (VARIANT H).  
RX MEDLINE=20154951; PubMed=10690361;  
RA Han S.K., Shin Y.C., Byun H.D.;  
RT "Biochemical, molecular and physiological characterization of a new  
RT beta-casein variant detected in Korean cattle.";  
RL Anim. Genet. 31:49-51(2000).  
[14]  
RN SEQUENCE OF 125-195 (VARIANTS A1 AND G).  
RA Dong C., Ng-Kwai-Hang K.F.;  
RT "Characterization of a non-electrophoretic genetic variant of beta-  
RT casein by peptide mapping and mass spectrometric analysis.";  
RL Int. Dairy J. 8:967-972(1998).  
[15]  
RN SEQUENCE OF 160-171 (VARIANT F).  
RX MEDLINE=96118672; PubMed=7496485;  
RA Visser S., Slangen C.J., Lagerwerf F.M., Van Dongen W.D.,  
RA Haverkamp J.;  
RT "Identification of a new genetic variant of bovine beta-casein using  
RT reversed-phase high-performance liquid chromatography and mass  
RT spectrometric analysis.";  
RL J. Chromatogr. A 711:141-150(1995).  
[16]  
RN SEQUENCE OF 170-184 FROM N.A.  
RX MEDLINE=83182023; PubMed=6897774;  
RA Willis I.M., Stewart A.F., Caputo A., Thompson A.R., McKinlay A.G.;  
RT "Construction and identification by partial nucleotide sequence  
RT analysis of bovine casein and beta-lactoglobulin cDNA clones.";  
RL DNA 1:375-386(1982).  
[17]  
RN CARBOHYDRATE-LINKAGE SITES.  
RX MEDLINE=85000478; PubMed=6148101;  
RA Yan S.B., Wold F.;  
RT "Neoglycoproteins: in vitro introduction of glycosyl units at  
RT glutamines in beta-casein using transglutaminase.";  
RL Biochemistry 23:3759-3765(1984).

CC -!- FUNCTION: IMPORTANT ROLE IN DETERMINATION OF THE SURFACE  
CC PROPERTIES OF THE CASEIN MICELLES.  
CC -!- SUBCELLULAR LOCATION: Extracellular.  
CC -!- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.  
CC -!- POLYMORPHISM: LEU-152 IS PRESENT IN THE VARIANTS F AND G; GLN-190  
CC AND GLU-210 ARE PRESENT IN THE VARIANT H. THE SEQUENCE SHOWN IS  
CC THE A2 VARIANT.  
CC -!- SIMILARITY: BELONGS TO THE BETA-CASEIN FAMILY.  
CC -!- DATABASE: NAME-Protein Spotlight;  
CC NOTE=Issue 16 of November 2001;  
CC WWW="http://www.expasy.org/spotlight/articles/sptlt016.html".  
CC  
CC This SWISS-PROT entry is copyright. It is produced through a collaboration  
CC between the Swiss Institute of Bioinformatics and the EMBL outstation -  
CC the European Bioinformatics Institute. There are no restrictions on its  
CC use by non-profit institutions as long as its content is in no way  
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CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
CC  
CC EMBL; M16645; AAA30480.1; -  
CC EMBL; M15132; AAA30430.1; -  
CC EMBL; K01087; AAA30481.1; -  
CC EMBL; X06359; CAA29658.1; -  
CC EMBL; M55158; AAA30431.1; -  
CC EMBL; S67277; AAB29137.1; -  
CC EMBL; AF104929; AAD09813.1; -  
CC EMBL; AF104928; AAD09813.1; JOINED.  
CC EMBL; M64756; AAB59254.1; -  
CC PIR; A03110; KBOA2.  
CC PIR; A25846; A25846.  
CC PIR; B29087; B29087.  
CC PIR; S01860; S01860.  
CC PIR; S02429; S02429.  
CC CarBank; CCSD:9067; -  
CC InterPro; IPR001588; Casein.  
CC Pfam; PF00363; caseins; 1.  
CC PROSITE; PS00306; CASEIN\_ALPHA\_BETA; 1.  
CC Milk; Phosphorylation; Glycoprotein; Signal; Polymorphism.  
KW  
FT SIGNAL 1 15  
FT CHAIN 16 224 BETA CASEIN.  
FT MOD\_RES 30 30 PHOSPHORYLATION.  
FT MOD\_RES 32 32 PHOSPHORYLATION.  
FT MOD\_RES 33 33 PHOSPHORYLATION.  
FT MOD\_RES 34 34 PHOSPHORYLATION.  
FT MOD\_RES 50 50 PHOSPHORYLATION (EXCEPT IN VARIANT C).  
FT CARBOHYD 70 72 O-LINKED (GALNAC. . .) (PARTIAL).  
FT CARBOHYD 72 72 O-LINKED (GALNAC. . .).  
FT CARBOHYD 95 95 O-LINKED (GALNAC. . .).  
FT CARBOHYD 183 183 O-LINKED (GALNAC. . .).  
FT VARIANT 40 40 R -> C (IN VARIANT H).  
FT VARIANT 51 51 E -> K (IN VARIANT E).  
FT VARIANT 52 52 E -> K (IN VARIANT C).  
FT VARIANT 82 82 P -> H (IN VARIANTS A1, B, C, F AND G).  
FT VARIANT 103 103 L -> I (IN VARIANT H).  
FT VARIANT 121 121 H -> Q (IN VARIANT A3).  
FT VARIANT 132 132 E -> Q (IN VARIANTS A1 AND G).  
FT VARIANT 137 137 S -> R (IN VARIANT B).  
FT VARIANT 152 153 LP -> PL (IN VARIANTS A1 AND H).  
FT VARIANT 153 153 P -> L (IN VARIANT G).  
FT VARIANT 167 167 P -> L (IN VARIANT F).  
FT VARIANT 190 190 Q -> E (IN VARIANTS A1 AND G).  
FT CONFLICT 108 108 M -> L (IN REF. 4 AND 7).  
FT CONFLICT 210 210 E -> Q (IN REF. 4 AND 7).  
FT CONFLICT 215 224 PVKGFPIIV -> DPSLLI (IN REF. 1).  
SQ SEQUENCE 224 AA; 25107 MW; F0BDD8148A238AE CRC64;  
P02666 Length: 224 February 28, 2003 14:33 Type: P Check: 8112 ..  
Initial Score = 12 Optimized Score = 12 Significance = 1.33  
Residue Identity = 100% Matches = 12 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0

X 10 X  
SLVYPPFGPIPN  
|||||  
DKIHFAQTOSLVYPPFGPIPNSLPONIPPLT  
70 X 80 X 90

#### 4. US-09-095-639A-4 (1-12) Bovine beta casein variant A1 immunogenic peptide.

W31289

ID W31289 standard; peptide; 12 AA.

AC W31289;  
DT 05-MAR-1998 (first entry)  
DE Bovine beta casein variant A1 immunogenic peptide.  
KW A1 variant beta casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
PN WO9724371-A1.  
PD 10-JUL-1997.

27-DEC-1996; E05846.

27-DEC-1995; IT-RM0850.

(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

(MIDI-) MIDIA LTD.

PI Pozzilli P;

DR WPI; 97-363622/33.

PT Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

PS Claim 5; Page 3; 34pp; English.

CC This sequence represents an immunogenic peptide from the A1 variant of beta-casein which contains a motif (see W31287) capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

SQ Sequence 12 AA:

SQ 0 A; 0 R; 1 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 1 H;  
SQ 1 I; 1 L; 0 K; 0 M; 1 F; 3 P; 1 S; 0 T; 0 W; 1 Y; 1 V;  
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 11 Optimized Score = 11 Significance = 1.06  
Residue Identity = 91% Matches = 11 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X 10 X  
SLVYPPFGPIPN  
|||||  
SLVYPPFGPIPN  
X 10 X

#### 5. US-09-095-639A-4 (1-12) Bovine beta casein variant A1 immunogenic peptide.

TOIG of: aaw31289 check: 5975 from: 1 to: 12

ID AAW31289 standard; peptide; 12 AA.

AC AAW31289;

DT 05-MAR-1998 (first entry)

DE Bovine beta casein variant A1 immunogenic peptide.

KW A1 variant beta casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.

OS Bos taurus.

PN WO9724371-A1.  
XX 10-JUL-1997.  
XX 27-DEC-1996; 96WO-EP05846.  
XX 27-DEC-1995; 95IT-ORM0850.  
XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
XX (MIDI-) MIDIA LTD.  
XX Pozzilli P;  
XX WPI; 1997-363622/33.

XX Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

PS Claim 5; Page 3; 34pp; English.

CC This sequence represents an immunogenic peptide from the A1 variant of beta-casein which contains a motif (see AAW31287) capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

SQ Sequence 12 AA;

AAW31289 Length: 12 March 3, 2003 11:28 Type: P Check: 5975

Initial Score = 11 Optimized Score = 11 Significance = 1.06  
Residue Identity = 91% Matches = 11 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X 10 X  
SLVYPPFGPIPN  
|||||  
SLVYPPFGPIPN  
X 10 X

#### 6. US-09-095-639A-4 (1-12) Bovine beta casein A1 variant.

ID R95609 standard; protein; 209 AA.

AC R95609;

DT 26-NOV-1996 (first entry)

DE Bovine beta casein A1 variant.

KW Milk; beta casein; diabetogenic; diabetes; cow; milk products;

KW butter; cheese; cream.

OS Bos taurus.

FH Key Location/Qualifiers

FT region 63..68

FT WO9614577-A1.

PD 17-MAY-1996.

PF 03-NOV-1995; NZ0114.

PR 04-NOV-1994; NZ-264862.

PA (NACH-) NAT CHILD HEALTH RES FOUND.

PA (NZDA-) NEW ZEALAND DAIRY BOARD.

PI Elliott RB, Hill JP;

DR WPI; 96-251885/25.

PT Selecting non-diabetogenic milk and milk prods. - by testing milk or cows for the presence of non-diabetogenic variants of beta-casein

PT Disclosure; Figure 2; 28pp; English.

PS A method for selecting milk for feeding to diabetes susceptible

CC individuals comprises testing milk from identified cows for the



CC presence of variants of beta casein and selecting those cows whose  
CC milk contains non-diabetogenic variants and milking these cows  
CC separately. The milk and milk products obtained can reduce the risk  
CC of susceptible individuals contracting Type-1 diabetes.

SO Sequence 209 AA;

5 A: 4 R: 4 N: 5 D: 0 B: 0 C: 21 Q: 18 E: 0 Z: 5 G: 6 H;

SO 10 I: 22 L: 11 K: 6 M: 9 F: 34 P: 16 S: 9 T: 1 W: 4 Y: 19 V;

CC Retrieved by boobyren on Thu 27 Feb 103 16:22:05 PST using FindSeq

Initial Score = 11 Optimized Score = 11 Significance = 1.06  
Residue Identity = 91% Matches = 11 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X 10 X  
SLVYPPFGPIPN  
|||||  
DKIHFAQTSLVYPPFGPIHNSLPQNIPLPT  
50 X 60 70

us-09-095-639a-4 (1-12)  
R80281 Methyl or ethyl esterified bovine beta-casein A1.

ID R80281 standard; protein; 209 AA.

AC R80281;

DT 14-FEB-1996 (first entry)

DE Methyl or ethyl esterified bovine beta-casein A1.

KW Bovine; beta-casein; ethyl esterification; pepsin hydrolysis;

KW proteolysis; peptide ester; food; pharmaceutical; cosmetics.

OS Bos taurus.

FT Key

FT Location/Qualifiers

FT 1..209

FT /note= "5% esterified by methanol or by

FT ethanol, resulting in atypical pepsin

FT cleavage sites, in addition to the

FT naturally occurring (native) sites"

FT 4..5

FT /note= "pepsin cleavage site in native protein"

FT 5..6

FT /note= "pepsin cleavage site in native protein and

FT in methyl ester of beta-casein"

FT 11..12

FT /note= "newly identified pepsin cleavage site in

FT methyl ester of beta-casein"

FT 15..16

FT /note= "pepsin cleavage site in native protein"

FT 44..45

FT /note= "pepsin cleavage site in native protein"

FT 45..46

FT /note= "pepsin cleavage site in native protein and

FT in ethyl ester of beta-casein"

FT 55..56

FT /note= "pepsin cleavage site in native protein and

FT in ethyl ester of beta-casein"

FT 57..58

FT /note= "pepsin cleavage site in native protein and

FT in ethyl ester of beta-casein"

FT 58..59

FT /note= "pepsin cleavage site in native protein and

FT in ethyl ester of beta-casein"

FT 72..73

FT /note= "pepsin cleavage site in native protein"

FT 73..74

FT /note= "newly identified pepsin cleavage site in

FT methyl ester of beta-casein"

FT 80..81

FT /note= "pepsin cleavage site in native protein and

FT in ethyl ester of beta-casein"

FT 93..94

FT /note= "pepsin cleavage site in native protein and

FT in methyl and ethyl esters of beta-casein"

FT 125..126

FT /note= "pepsin cleavage site in native protein"

FT

FT cleavage\_site 126..127  
FT /note= "pepsin cleavage site in native protein"  
FT cleavage\_site 127..128  
FT /note= "pepsin cleavage site in native protein"  
FT cleavage\_site 141..142  
FT /note= "pepsin cleavage site in native protein"  
FT cleavage\_site 142..143  
FT /note= "pepsin cleavage site in native protein and  
FT in methyl and ethyl esters of beta-casein"  
FT cleavage\_site 156..157  
FT /note= "newly identified pepsin cleavage site in  
FT ethyl ester of beta-casein"  
FT cleavage\_site 162..163  
FT /note= "newly identified pepsin cleavage site in  
FT ethyl ester of beta-casein"  
FT cleavage\_site 163..164  
FT /note= "pepsin cleavage site in native protein and  
FT in methyl and ethyl esters of beta-casein"  
FT cleavage\_site 164..165  
FT /note= "pepsin cleavage site in native protein and  
FT in ethyl ester of beta-casein"  
FT cleavage\_site 188..189  
FT /note= "pepsin cleavage site in native protein and  
FT in methyl ester of beta-casein"  
FT cleavage\_site 189..190  
FT /note= "pepsin cleavage site in native protein and  
FT in methyl and ethyl esters of beta-casein"  
FT cleavage\_site 190..191  
FT /note= "pepsin cleavage site in native protein and  
FT in ethyl ester of beta-casein"  
FT cleavage\_site 191..192  
FT /note= "pepsin cleavage site in native protein and  
FT in methyl and ethyl esters of beta-casein"  
FT cleavage\_site 192..193  
FT /note= "pepsin cleavage site in native protein and  
FT in methyl and ethyl esters of beta-casein"  
FT cleavage\_site 198..199  
FT /note= "newly identified pepsin cleavage site in  
FT methyl and ethyl esters of beta-casein"  
FT cleavage\_site 207..208  
FT /note= "newly identified pepsin cleavage site in  
FT methyl ester of beta-casein"  
FT peptide 2..25  
FT /label= A  
FT /note= "tryptic peptide from native protein"  
FT peptide 26..28  
FT /label= B  
FT /note= "tryptic peptide from native protein"  
FT peptide 29..32  
FT /label= C  
FT /note= "tryptic peptide from native protein"  
FT peptide 33..48  
FT /label= D  
FT /note= "tryptic peptide from native protein"  
FT peptide 49..97  
FT /label= E  
FT /note= "tryptic peptide from native protein"  
FT peptide 100..105  
FT /label= F  
FT /note= "tryptic peptide from native protein"  
FT peptide 106..107  
FT /label= G  
FT /note= "tryptic peptide from native protein"  
FT peptide 108..113  
FT /label= H  
FT /note= "tryptic peptide from native protein"  
FT peptide 114..169  
FT /label= I  
FT /note= "tryptic peptide from native protein"  
FT peptide 170..176  
FT /label= J  
FT /note= "tryptic peptide from native protein"  
FT peptide 177..183

FT	/label= K
FT	/note= "tryptic peptide from native protein"
FT	184..202
FT	/label= L
FT	/note= "tryptic peptide from native protein"
FT	203..209
FT	/label= N
FT	/note= "tryptic peptide from native protein"
FT	15
FT	modified_site
FT	17
FT	/note= "phosphorylated"
FT	17
FT	/note= "phosphorylated"
FT	18
FT	/note= "phosphorylated"
FT	19
FT	/note= "phosphorylated"
FT	35
FT	/note= "phosphorylated"
PN	W09517518-A1.
	29-JUN-1995.
	20-DEC-1995. FO1500.
PA	23-DEC-1993; FR-015764.
PI	(INRG ) INST NAT RECH AGRONOMIQUE.
PI	Briand L, Chobert J, Haertle T;
DR	WPI; 95-240679/31.
PT	New esterified amino acids, peptide(s) and their mixts. - prepd. by
PT	esterification of protein then enzymatic hydrolysis, useful as
PT	ingredients and additives in foods, pharmaceuticals and cosmetics
PS	Claim 7; Fig 7 and 18; 47pp; French.
CC	The native form of bovine beta-casein Al contains various pepsin
CC	cleavage sites. Esterification of the protein with methanol or ethanol
CC	results in a form of beta-casein contg. additional, non-conventional
CC	pepsin cleavage sites (see Features Table). Esterified peptides and
CC	amino acids (and their mixtures) resulting from hydrolysis of an
CC	esterified protein (pref. beta-lactoglobulin or beta-casein) are
CC	claimed. The hydrolysis products are useful as ingredients,
CC	additives or active agents in foods, pharmaceuticals and cosmetics.
CC	Sequence 209 AA;
5	A; 4 R; 5 N; 4 D; 0 B; 0 C; 20 Q; 19 E; 0 Z; 5 G; 6 H;
SQ	10 I; 22 L; 11 K; 6 M; 9 F; 34 P; 16 S; 9 T; 1 W; 4 Y; 19 V;
CC	Retrieved by bobryen on Thu 27 Feb 103 16:22:04-PST using FindSeq

B.	US-09-095-639A-4 (1-12)	
aar95609	Bovine beta casein A1 variant.	
TOIG of:	aar95609	check: 2014 from: 1 to: 209
ID	AAR95609	standard; protein; 209 AA.
XX		
AC	AAR95609;	
XX		
DT	26-NOV-1996	(first entry)
XX		
DE	Bovine beta casein A1 variant.	
XX		
KW	Milk; beta casein; diabetogenic; diabetes; cow; milk products;	
KW	butter; cheese; cream.	
XX		
OS	Bos taurus.	
XX		
Key	Location/Qualifiers	
FH	Region	63. .68
FT		

FT	/label= Diabetogenic hexapeptide.			
XX	PN	WO9614577-A1.		
XX	PD	17-MAY-1996.		
XX	PF	03-NOV-1995;	95WO-NZ00114.	
XX	PR	04-NOV-1994;	94NZ-0264862.	
XX	PA	(NACH-) NAT CHILD HEALTH RES FOUND.		
XX	PA	(NZDA-) NEW ZEALAND DAIRY BOARD.		
XX	PI	Elliott RB,	Hill JP;	
XX	DR	WPI; 1996-251885/25.		
XX	FT	Selecting non-diabetogenic milk and milk prods. - by testing milk or		
XX	PT	cows for the presence of non-diabetogenic variants of beta-casein		
XX	XX	Disclosure; Figure 2; 28pp; English.		
XX	CC	A method for selecting milk for feeding to diabetes susceptible		
XX	CC	individuals comprises testing milk from identified cows for the		
XX	CC	presence of variants of beta casein and selecting those cows whose		
XX	CC	milk contains non-diabetogenic variants and milking these cows		
XX	CC	separately. The milk and milk products obtained can reduce the risk		
XX	CC	of susceptible individuals contracting Type-1 diabetes.		
XX	SQ	Sequence	209 AA;	
		AAR95609	Length: 209	March 3, 2003 11:28 Type: P Check: 2014 ..
		Initial Score	= 11	Optimized Score = 11 Significance = 1.06
		Residue Identity	= 91%	Matches = 11 Mismatches = 1
		gaps	= 0	Conservative Substitutions = 1

9.	US-09-095-639A-4 (1-12)	Bovine beta casein variant A2 immunogenic peptide
W31288		
ID	W31288	standard; peptide; 5 AA.
AC	W31288;	
DT	05-MAR-1998	(first entry)
DE	Bovine beta casein variant A2 immunogenic peptide motif.	
DE	A2 variant beta-casein; immunogenic; molecular mimicry; cow;	
KW	milk product; insulin-dependent diabetes; GLUT2; diet.	
KW	Bos taurus.	
OS	Bos indicus	
OS	Bos indicus	
PN	WO9724371-A1.	
PD	10-JUL-1997.	
PF	27-DEC-1996;	E05846.
PR	27-DEC-1995;	IT-RM0850.
PA	(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.	
PA	(MIDI-) MIDIA LTD.	
PI	Pozzilli P.	
PI	WPI: 97-363622/33.	
DR	Beta-casein or fragments not showing mimicry with GLUT2 - used in	
PT	food or pharmaceutical products for prevention of insulin dependent	
PT	diabetes, particularly in early infancy	
PT	Claim 5; Page 4; 34pp; English.	
CC	This sequence represents an immunogenic peptide motif from the A2 variant	
CC	beta-casein found in both Bos taurus and Bos indicus (amino acid	
CC	position 63-68). This motif is capable of mimicking a fragment of the	
CC	GLUT2 protein found in insulin producing cells of the pancreas. There is	
CC	a known correlation between exposure to cow's milk and the development of	
CC	insulin-dependent diabetes which could possibly be linked to this	
CC		

CC molecular mimicry. Dietary or pharmaceutical products derived from milk  
 CC substantially free of non-human beta casein or containing modified  
 CC beta-casein without this motif could be used in diets for the prevention  
 CC of insulin dependent diabetes particularly during early infancy.  
 SQ Sequence 5 AA;  
 SQ 0 A; 0 R; 0 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 0 H;  
 SQ 1 I; 0 L; 0 K; 0 M; 0 F; 3 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
 CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 5 Optimized Score = 5 Significance = -0.53  
 Residue Identity = 100% Matches = 5 Mismatches = 0  
 Gaps = 0 Conservative Substitutions = 0

X 10  
 SLVYPPFGPIP  
 |||||  
 PGPIP  
 X X

US-09-095-639A-4 (1-12)  
 aaw31288 Bovine beta casein variant A2 immunogenic peptide

TOIG of: aaw31288 check: 1154 from: 1 to: 5

ID AAW31288 standard; peptide; 5 AA.

AC AAW31288;

DT 05-MAR-1998 (first entry)

DE Bovine beta casein variant A2 immunogenic peptide motif.

KW A2 variant beta-casein; immunogenic; molecular mimicry; cow;  
 KW milk product; insulin-dependent diabetes; GLUT2; diet.

OS Bos taurus.

XX Bos indicus

XX WO9724371-A1.

XX 10-JUL-1997.

XX 27-DEC-1996; 96WO-EP05846.

XX 27-DEC-1995; 95IT-OR0850.

XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
 XX (MIDI-) MIDIA LTD.

XX Pozzilli P;

XX WPI; 1997-363622/33.

XX Beta-casein or fragments not showing mimicry with GLUT2 - used in  
 XX food or pharmaceutical products for prevention of insulin dependent  
 XX diabetes, particularly in early infancy

XX Claim 5; Page 4; 34pp; English.

XX This sequence represents an immunogenic peptide motif from the A2 variant  
 CC beta-casein found in both Bos taurus and Bos indicus (amino acid  
 CC position 63-68). This motif is capable of mimicking a fragment of the  
 CC GLUT2 protein found in insulin producing cells of the pancreas. There is  
 CC a known correlation between exposure to cow's milk and the development of  
 CC insulin-dependent diabetes which could possibly be linked to this  
 CC molecular mimicry. Dietary or pharmaceutical products derived from milk  
 CC substantially free of non-human beta casein or containing modified  
 CC beta-casein without this motif could be used in diets for the prevention  
 CC of insulin dependent diabetes particularly during early infancy.

SQ Sequence 5 AA;

AAW31288 Length: 5 March 3, 2003 11:28 Type: P Check: 1154  
 Initial Score = 5 Optimized Score = 5 Significance = -0.53  
 Residue Identity = 100% Matches = 5 Mismatches = 0  
 Gaps = 0 Conservative Substitutions = 0

X 10  
 SLVYPPFGPIP  
 |||||  
 PGPIP  
 X X

11. US-09-095-639A-4 (1-12)  
 p02662 Alpha-S1 casein precursor.

TOIG of: p02662 check: 2471 from: 1 to: 214

ID CAS1\_BOVIN STANDARD; PRT; 214 AA.

AC P02662; Q28048;

DT 21-JUL-1986 (Rel. 01, Created)

DT 01-NOV-1990 (Rel. 16, Last sequence update)

DT 01-MAR-2002 (Rel. 41, Last annotation update)

DE Alpha-S1 casein precursor.

GN CSNIS1.

OS Bos taurus (Bovine).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;

OC Bovidae; Bovinae; Bos.

OX NCBI\_TaxID=9913;

RN [1]

RP SEQUENCE FROM N.A.

RX MEDLINE=84221403; PubMed=6328443;

RA Stewart A.F., Willis I.M., Mackinlay A.G.;

RT "Nucleotide sequences of bovine alpha S1- and kappa-casein cDNAs."

RL Nucleic Acids Res. 12:3895-3907(1984).

RN [2]

RP SEQUENCE FROM N.A.

RA Nagao M., Maki M., Sasaki R., Chiba R.;

RT "Isolation and sequence analysis of bovine alpha-S1-casein cDNA

clone."

RL Agric. Biol. Chem. 48:1663-1667(1984).

RN [3]

RP SEQUENCE FROM N.A.

RX MEDLINE=87049835; PubMed=3022833;

RA Gorodetskii S.I., Zakhar'ev V.M., Kyarshulite D.R., Kapelinskaya T.V.,

RT "cDNA of cattle alpha S1-casein: cloning and nucleotide sequence."

RL Biokhimiia 51:1641-1648(1986).

RN [4]

RP SEQUENCE FROM N.A.

RX MEDLINE=92051301; PubMed=1658736;

RA Koczan D., Hobom G., Seyfert H.M.;

RT "Genomic organization of the bovine alpha-S1 casein gene."

RL Nucleic Acids Res. 19:5591-5596(1991).

RN [5]

RP SEQUENCE OF 55-130 FROM N.A.

RX MEDLINE=83182023; PubMed=6897774;

RA Willis I.M., Stewart A.F., Caputo A., Thompson A.R., McKinlay A.G.;

RT "Construction and identification by partial nucleotide sequence

analysis of bovine casein and beta-lactoglobulin cDNA clones."

RL DNA 1:375-386(1982).

RN [6]

RP SEQUENCE OF 122-214 FROM N.A.

RX MEDLINE=85178933; PubMed=3838718;

RA Kyarshulite D.R., Zakhar'ev V.M., Gorodetskii S.I.;

RT "Nucleotide sequence of the 3'-nontranslated region of the mRNA of

alpha S1-casein in cows."

RL Dokl. Akad. Nauk SSSR 280:1433-1437(1985).

RN [7]

RP SEQUENCE OF 164-214 FROM N.A.

RX MEDLINE=94154154; PubMed=1343827;

RA Chen R., Wang B., Zhang Y., Liu W., Zhang J., Lao W.;

Mon Mar 3 11:50:09 2003

"Cloning, mapping, and sequencing of 3' and its flanking region of bovine alpha-s1 casein gene.";  
Chin. J. Biotechnol. 8:235-245(1992).  
[8]  
SEQUENCE OF 16-214 (VARIANT B).  
MEDLINE=72063417; PubMed=4331376;  
Mercier J.-C., Grosclaude F., Ribadeau-Dumas B.;  
"Primary structure of bovine alpha-s1 casein. Complete sequence.";  
Eur. J. Biochem. 23:41-51(1971).  
[9]  
REVIEWS TO 74 AND 92-93 (VARIANTS A; B; C AND D).  
MEDLINE=74082545; PubMed=4797901;  
Mercier J.-C., Grosclaude F., Ribadeau-Dumas B.;  
"Primary structure of alpha casein and of bovine beta casein.  
Correction.";  
Eur. J. Biochem. 40:323-323(1973).  
[10]  
SEQUENCE (VARIANT D).  
MEDLINE=72214259; PubMed=5064450;  
Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;  
"Characterization of genetic variants of alpha-s1 and beta bovine  
caseins.";  
Eur. J. Biochem. 26:328-337(1972).  
[11]  
SEQUENCE OF 23-49 (VARIANT A).  
Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;  
"Localization in the N-terminal part of bovine casein alpha-s1 of a  
13 amino-acid deletion that differentiates variant A from variants B  
and C.";  
FEBS Lett. 11:109-112(1970).  
[12]  
SEQUENCE OF 205-214 (VARIANT C).  
Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.;  
"On the localization in the C-terminal sequence of bovine casein  
alpha-s1 of a Glu/Gly substitution that differentiates the genetic  
variants B and C.";  
Eur. J. Acad. Sci., D, Sci. Nat. 268:3133-3136(1970).  
[13]  
REVISION (VARIANT C).  
Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.;  
C. R. Acad. Sci., D, Sci. Nat. 271:563-563(1970).  
- FUNCTION: IMPORTANT ROLE IN THE CAPACITY OF MILK TO TRANSPORT  
CALCIUM PHOSPHATE.  
- SUBCELLULAR LOCATION: Extracellular.  
- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.  
- MISCELLANEOUS: THE B VARIANT SEQUENCE IS SHOWN.  
- SIMILARITY: BELONGS TO THE ALPHA-CASEIN FAMILY.  
- DATABASE: NAME=Worthington enzyme manual;  
WWW="http://www.worthington-biochem.com/manual/C/CASA.html".  
- DATABASE: NAME=Protein Spotlight;  
NOTE=Issue 16 of November 2001;  
WWW="http://www.expasy.org/spotlight/articles/sptlt016.html".  
-----  
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EMBL; X00564; CAB57792.1; -  
EMBL; M33123; AAA30428.1; -  
EMBL; M38641; AAA30429.1; -  
EMBL; X59856; CAA42516.1; -  
EMBL; K01084; AAA30478.1; -  
EMBL; M38658; AAA62707.1; -  
EMBL; S72388; AAD14099.1; -  
PIR; A03106; KAOBSB.  
PIR; A23071; A23071.  
PIR; S02202; S02202.  
PIR; S22575; S22575.  
InterPro; IPR001588; Casein.

DR PFam; PF00363; caseins; 1.  
DR PROSITE; PS00306; CASEIN.ALPHA.BETA; 1.  
KW Milk; Phosphorylation; Signal; Repeat.  
FT SIGNAL 1 15  
FT CHAIN 16 214 ALPHA-S1 CASEIN.  
FT MOD\_RES 61 61 PHOSPHORYLATION.  
FT MOD\_RES 63 63 PHOSPHORYLATION.  
FT MOD\_RES 68 68 PHOSPHORYLATION (IN VARIANT D).  
FT MOD\_RES 79 79 PHOSPHORYLATION.  
FT MOD\_RES 81 81 PHOSPHORYLATION.  
FT MOD\_RES 82 82 PHOSPHORYLATION.  
FT MOD\_RES 83 83 PHOSPHORYLATION.  
FT MOD\_RES 90 90 PHOSPHORYLATION.  
FT MOD\_RES 130 130 PHOSPHORYLATION.  
FT REPEAT 125 140  
FT VARIAT 29 41 MISSING (IN VARIANT A).  
FT VARIAT 68 68 A -> T (IN VARIANT D).  
FT VARIAT 207 207 E -> G (IN VARIANT C).  
FT CONFLICT 42 42 P -> L (IN REF. 3).  
FT CONFLICT 50 50 E -> Q (IN REF. 4 AND 11).  
FT CONFLICT 95 95 H -> Q (IN REF. 5).  
FT CONFLICT 143 143 H -> D (IN REF. 3).  
FT CONFLICT 203 203 S -> L (IN REF. 6).  
FT CONFLICT 211 212 MP -> IS (IN REF. 3).  
FT CONFLICT 214 214 MP -> IS (IN REF. 3).  
SQ SEQUENCE 214 AA; 24529 MW; F066B5C8AE55828B CRC64;

P03662 Length: 214 February 28, 2003 14:33 Type: P Check: 2471 ..

Initial Score = 5 Optimized Score = 7 Significance = -0.53  
Residue Identity = 25% Matches = 3 Mismatches = 8  
Gaps = 0 Conservative Substitutions = 1

X 10 X  
SLVTFPGPIPN  
| | | |  
QKEPMIGVNOELAYFPELFRQFYOLDAYPSG  
.150 X 160 170

12. US-09-095-639A-4 (1-12)

W31294 Bovine beta casein immunogenic peptide motif 2.

W31294 standard; peptide; 4 AA.

ID W31294;  
AC 05-MAR-1998 (first entry)  
DE Bovine beta casein immunogenic peptide motif 2.  
KW Beta-casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
PN WO9724371-A1.  
PD 10-JUL-1997.  
PR 27-DEC-1996; E05846.  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
PI Pozzilli P;  
DR WPI; 97-363622/33.  
PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
PT Claim 10; Page 6; 34pp; English.  
PS This sequence represents an immunogenic peptide motif found in bovine  
CC beta casein. This motif is capable of mimicking a fragment of the  
CC GLUT2 protein found in insulin producing cells of the pancreas. There is  
CC a known correlation between exposure to cow's milk and the development of  
CC insulin-dependent diabetes which could possibly be linked to this  
CC molecular mimicry. Dietary or pharmaceutical products derived from milk  
CC substantially free of non-human beta casein or containing modified  
CC beta-casein without this motif could be used in diets for the prevention  
CC of insulin dependent diabetes particularly during early infancy.  
SQ Sequence 4 AA;  
SQ 0 A; 0 R; 0 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 0 H;

SQ 1 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq  
Initial Score = 4 Optimized Score = -0.80  
Residue Identity = 100% Matches = 4 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0

10

SLVYPPFGPIP

||||

GPPI

X X

13. US-09-095-639A-4 (1-12)  
aaw31294 Bovine beta casein immunogenic peptide motif 2.

TOIG of: aaw31294 check: 770 from: 1 to: 4

AAW31294 standard; peptide: 4 AA.

AAW31294;

05-MAR-1998 (first entry)

Bovine beta casein immunogenic peptide motif 2.

Beta-casein; immunogenic; molecular mimicry; cow;  
milk product; insulin-dependent diabetes; GLUT2; diet.

Bos taurus.

WO9724371-A1.

10-JUL-1997.

27-DEC-1996; 96WO-EP05846.

27-DEC-1995; 95IT-OR0850.

(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

(MIDI-) MIDIA LTD.

Pozzilli P;

WPI; 1997-363622/33.

Beta-casein or fragments not showing mimicry with GLUT2 - used in  
food or pharmaceutical products for prevention of insulin dependent  
diabetes, particularly in early infancy

Claim 10; Page 6; 34pp; English.

This sequence represents an immunogenic peptide motif found in bovine  
beta casein. This motif is capable of mimicking a fragment of the  
GLUT2 protein found in insulin producing cells of the pancreas. There is  
a known correlation between exposure to cow's milk and the development of  
insulin-dependent diabetes which could possibly be linked to this  
molecular mimicry. Dietary or pharmaceutical products derived from milk  
substantially free of non-human beta casein or containing modified  
beta-casein without this motif could be used in diets for the prevention  
of insulin dependent diabetes particularly during early infancy.

Sequence 4 AA;

AAW31294 Length: 4 March 3, 2003 11:28 Type: P Check: 770 ..

Initial Score = 4 Optimized Score = -0.80  
Residue Identity = 100% Matches = 4 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0

10

SLVYPPFGPIP

||||  
GPPI  
X X

14. US-09-095-639A-4 (1-12)  
W31287 Bovine beta casein variant A1 immunogenic peptide

ID W31287 standard; peptide: 5 AA.

AC W31287;

05-MAR-1998 (first entry)

Bovine beta casein variant A1 immunogenic peptide motif.

Al variant beta casein; immunogenic; molecular mimicry; cow;  
milk product; insulin-dependent diabetes; GLUT2; diet.

Bos taurus.

WO9724371-A1.

10-JUL-1997.

27-DEC-1996; E05846.

27-DEC-1995; IT-RM0850.

(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

(MIDI-) MIDIA LTD.

Pozzilli P;

WPI; 97-363622/33.

Beta-casein or fragments not showing mimicry with GLUT2 - used in  
food or pharmaceutical products for prevention of insulin dependent  
diabetes, particularly in early infancy

Claim 5; Page 3; 34pp; English.

This sequence represents an immunogenic peptide motif from the A1  
variant of beta-casein which is capable of mimicking a fragment of the  
GLUT2 protein found in insulin producing cells of the pancreas. There is  
a known correlation between exposure to cow's milk and the development of  
insulin-dependent diabetes which could possibly be linked to this  
molecular mimicry. Dietary or pharmaceutical products derived from milk  
substantially free of non-human beta casein or containing modified  
beta-casein without this motif could be used in diets for the prevention  
of insulin dependent diabetes particularly during early infancy.

Sequence 5 AA;

0 A; 0 R; 0 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 1 H;  
SQ 1 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 4 Optimized Score = -0.80  
Residue Identity = 80% Matches = 4 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X 10

SLVYPPFGPIP

||||

GPPI

X X

15. US-09-095-639A-4 (1-12)  
aaw31287 Bovine beta casein variant A1 immunogenic peptide

TOIG of: aaw31287 check: 1114 from: 1 to: 5

ID AAW31287 standard; peptide: 5 AA.

XX

AC AAW31287;

XX

05-MAR-1998 (first entry)

Bovine beta casein variant A1 immunogenic peptide motif.

Al variant beta casein; immunogenic; molecular mimicry; cow;  
milk product; insulin-dependent diabetes; GLUT2; diet.

Bos taurus.

WO9724371-A1.

10-JUL-1997.

PD

XX 27-DEC-1996; 96WO-EP05846.  
XX 27-DEC-1995; 95IT-ORM0850.  
XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
XX (MIDI-) MIDIA LTD.  
XX Pozzilll P;  
XX WPI; 1997-363622/33.  
XX Beta-casein or fragments not showing mimicry with GLUT2 - used in  
XX food or pharmaceutical products for prevention of insulin dependent  
XX diabetes, particularly in early infancy  
XX Claim 5; Page 3; 34pp; English.  
XX This sequence represents an immunogenic peptide motif from the A1  
XX variant of beta-casein which is capable of mimicking a fragment of the  
XX GLUT2 protein found in insulin producing cells of the pancreas. There is  
XX a known correlation between exposure to cow's milk and the development of  
XX insulin-dependent diabetes which could possibly be linked to this  
XX molecular mimicry. Dietary or pharmaceutical products derived from milk  
XX substantially free of non-human beta casein or containing modified  
XX beta-casein without this motif could be used in diets for the prevention  
XX of insulin dependent diabetes particularly during early infancy.  
XX SQ Sequence 5 AA;

AAW31287 Length: 5 March 3, 2003 11:29 Type: P Check: 1114 ..  
Initial Score = 4 Optimized Score = 4 Significance = -0.80  
Residue Identity = 80% Matches = 4 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X 10  
SLVYPPFGPIPN  
||||  
PGPIH  
X X

16. US-09-095-639A-4 (1-12)  
R37103 Bovine milk beta-casein enzymatic fragment.  
R37103 standard; peptide; 7 AA.

ID 21-MAY-1995 (first entry)  
AC Bovine milk beta-casein enzymatic fragment.  
KW Beta-casein; enzymatic hydrolysate; cosmetics; skin disorders;  
KW wrinkles.  
OS Bos Taurus.  
PN J06166615-A.  
PD 14-JUN-1994.  
PF 01-DEC-1992; 321624.  
PR 01-DEC-1992; JP-321624.  
PA (POKK) POLA CHEM IND INC.  
DR WPI; 94-230615/28.  
PT Cosmetics for treating skin disorders and wrinkles - containing  
PT enzymatic hydrolysate of human or bovine milk beta-casein  
PS Claim 2; Page 2; 7pp; Japanese.  
CC The invention relates to cosmetics containing human or bovine milk  
CC beta-casein enzymatic hydrolysate. The cosmetics are used for  
CC improving skin disorders and/or wrinkles. They are more effective  
CC than previously used polysaccharides, sugar alcohols, glycerol,  
CC glycols, etc.  
CC The present sequence is one component of the bovine milk beta-casein  
CC enzymatic hydrolysate.  
SQ Sequence 7 AA:  
SQ 1 A; 1 R; 0 N; 0 D; 0 B; 0 C; 1 Q; 0 E; 0 Z; 0 G; 0 H;  
SQ 0 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 1 Y; 1 V;  
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:04-PST using FindSeq

Initial Score = 4 Optimized Score = 4 Significance = -0.80  
Residue Identity = 28% Matches = 2 Mismatches = 4  
Gaps = 0 Conservative Substitutions = 1

X 10  
SLVYPPFGPIPN  
|:  
AVYPQOR  
X X

17. US-09-095-639A-4 (1-12)  
W31293 Bovine beta casein immunogenic peptide motif 1.

ID W31293 standard; peptide; 4 AA.  
AC W31293;  
DT 05-MAR-1998 (first entry)  
DE Beta casein immunogenic peptide motif 1.  
KW Beta casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
PN WO9724371-A1.  
PD 10-JUL-1997.  
PF 27-DEC-1996; E05846.  
PR 27-DEC-1995; IT-RM0850.  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
PI Pozzilll P;  
DR WPI; 97-363622/33.  
PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
PS Claim 10; Page 6; 34pp; English.  
CC This sequence represents an immunogenic peptide motif of beta-casein  
CC which is capable of mimicking a fragment of the GLUT2 protein found in  
CC insulin producing cells of the pancreas. There is a known correlation  
CC between exposure to cow's milk and the development of insulin-dependent  
CC diabetes which could possibly be linked to this molecular mimicry.  
CC Dietary or pharmaceutical products derived from milk substantially free  
CC of non-human beta casein or containing modified beta-casein without this  
CC motif could be used in diets for the prevention of insulin dependent  
CC diabetes particularly during early infancy.  
SQ Sequence 4 AA:  
SQ 0 A; 0 R; 0 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 1 H;  
SQ 1 I; 0 L; 0 K; 0 M; 0 F; 1 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 3 Optimized Score = 3 Significance = -1.06  
Residue Identity = 75% Matches = 3 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

10  
SLVYPPFGPIPN  
|||  
GPIH  
X X

18. US-09-095-639A-4 (1-12)  
aaw31293 Bovine beta casein immunogenic peptide motif 1.

TOIG of: aaw31293 check: 738 from: 1 to: 4

ID AAW31293 standard; peptide; 4 AA.

XX AAW31293;

XX 05-MAR-1998 (first entry)

DE Bovine beta casein immunogenic peptide motif 1.

XX Beta casein; immunogenic; molecular mimicry; cow;

KW milk product; insulin-dependent diabetes; GLUT2; diet.

XX OS

XX Bos taurus.

XX PN W09724371-A1.

XX PD 10-JUL-1997.

XX PF 27-DEC-1996; 96WO-EP05846.

XX PR 27-DEC-1995; 95IT-ORM0850.

XX PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

XX PD (MIDI-) MIDIA LTD.

XX PI Pozzilli P;

XX DR WPI; 1997-363622/33.

XX PT Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

XX PS Claim 10; Page 6; 34pp; English.

XX CC This sequence represents an immunogenic peptide motif of beta-casein which is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry.

XX CC Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

XX SQ Sequence 4 AA;

AAW31293 Length: 4 March 3, 2003 11:29 Type: P Check: 738 ..

Initial Score = 3 Optimized Score = -1.06  
Residue Identity = 75% Matches = 3 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

10

SLVYPPFGPIPN

|||

GPIH

X X

